TRANSACTIONS

OF THE

AMERICAN ASSOCIATION OF GENITO-URINARY SURGEONS

VOLUME XXVII

TRANSACTIONS

OF THE

AMERICAN ASSOCIATION OF GENITO-URINARY SURGEONS

Forty-sixth Annual Meeting held at
Hot Springs, Virginia

May 14, 15, and 16, 1934

Volume XXVII

Published for the Association by
The Bruce Publishing Company
Saint Paul and Minneapolis
1934

OFFICERS OF THE ASSOCIATION FOR 1933-1934

President

JOHN R. CAULK, M.D., St. Louis

Vice-President

ROBERT C. BRYAN, M.D., Richmond

Secretary-Treasurer

HENRY L. SANFORD, M.D., Cleveland
1622 Keith Building

Members of the Council

HARRY A. FOWLER, M.D., Washington, D.C.
HERMAN L. KRETSCHMER, M.D., Chicago
ARTHUR H. CROSBIE, M.D., Boston
THE PRESIDENT
THE VICE-PRESIDENT } *Ex-Officio*
THE SECRETARY

JUL 7 '47 U OF M BINDERY (13-M)

1168381

LIST OF MEMBERS

HONORARY MEMBERS

Dr. Gardner W. Allen (1893), 146 Massachusetts Ave., Boston.
Dr. George E. Brewer (1890), 19 East 65th Street, New York.
Dr. Charles L. Gibson (1901), 72 East 54th Street, New York.
Dr. Edward Martin (1892), 135 South 18th St., Philadelphia.
Dr. Abner Post* (1887), 130 Brattle St., Cambridge, Mass.
Dr. Paul Thorndike (1892), 24 Marlborough Street, Boston.
Dr. Francis S. Watson (1888), South Dartmouth, Mass.
Dr. William N. Wishard (1889), 1711 N. Capitol Ave., Indianapolis.

CORRESPONDING MEMBERS

Mr. E. Hurry Fenwick, C.B.E., F.R.C.S. (1906), 53 Bedford Gardens, Campden Hill, London, W. 8.
Prof. Serg. Petr. Fedrov (1911), Leningrad, Russia.
Prof. Emile Jeanbrau (1911), 1 Rue Barthez, Montpelier, France.
Mr. Frank Kidd, M.B., M.Ch., F.R.C.S. (1923), 55 Harley Street, London, W. 1.
Prof. Felix Legueu (1929), 4 Rue Henri-Moissan, Paris VII, France.
Prof. Dr. Med. A. von Lichtenberg (1929), Marburger Str., 3, Berlin, Germany.
Mr. John Pardoe, M.B., C.M., F.R.C.S. (1909), 1 Red House, Port Erroll, Aberdeen, Scotland.
Prof. Alfred Pousson (1909), 10 Cours Tournon, Bordeaux, France.
Prof. César Roux (1911), 3 Place Montbenon, Riant-Site, Lausanne, Switzerland.
Prof. Jean René Verhoegen (1911), 98 Rue Marie Thérèse, Brussels, Belgium.
Sir John W. Thomson-Walker, O.B.E., M.A., M.B., Ch.B., F.R.C.S. (1921), 96 Harley Street, London, W. 1.
Prof. Dr. Med. Hans Wildbolz (1929), 12 Finkenhubelweg, Berne, Switzerland.

FELLOWS

Dr. Robert C. Bryan (1915), 1108 West Franklin Street, Richmond, Va.
Dr. Hugh Cabot (1907), Mayo Clinic, Rochester, Minn.
Dr. Charles H. Chetwood (1900), 25 Park Avenue, New York.
Dr. Arthur L. Chute* (1909), 352 Marlborough Street, Boston.
Dr. J. Bayard Clark (1906), 140 East 54th Street, New York.
Dr. A. J. Crowell (1921), Professional Building, Charlotte, N. C.
Dr. H. A. Fowler (1907), 208 Stoneleigh Court, Washington, D. C.
Dr. Robert H. Greene* (1897), 78 East 56th Street, New York.

*Deceased.

Dr. Francis R. Hagner (1906), 209 Columbia Medical Building, Washington, D. C.
Dr. Edward L. Keyes (1901), 121 East 60th Street, New York.
Dr. Bransford Lewis (1892), 609 Humboldt Building, St. Louis.
Dr. William E. Lower (1912), 2050 East 93rd Street, Cleveland.
Dr. J. F. McCarthy (1924), 2 East 54th Street, New York.
Dr. Henry H. Morton (1900), 32 Schermerhorn Street, Brooklyn.
Dr. Harvey G. Mudd* (1887), 1017 Beaumont Medical Bldg., St. Louis.
Dr. Richard F. O'Neil (1909), 379 Beacon Street, Boston.
Dr. Alfred T. Osgood (1906), 65 E. 66th Street, New York.
Dr. James Pedersen (1906), 30 East 40th Street, New York.
Dr. E. W. Ruggles (1905), 348 University Avenue, Rochester, N. Y.
Dr. Henry L. Sanford (1916), 1622 Keith Building, Cleveland.
Dr. Louis E. Schmidt (1903), The Mallers Building, Chicago.
Dr. E. H. Siter (1913), Medical Arts Building, Philadelphia.
Dr. J. Bentley Squier (1906), 8 East 68th Street, New York.
Dr. Alfred C. Wood (1900), 2035 Walnut Street, Philadelphia.
Dr. Hugh H. Young (1901), Johns Hopkins Hospital, Baltimore.

ACTIVE MEMBERS

Dr. Nathaniel G. Alcock (1922), 201 Dey Building, Iowa City, Ia.
Dr. J. Dellinger Barney (1912), 87 Marlborough Street, Boston.
Dr. Benjamin S. Barringer (1911), 172 East 79th Street, New York.
Dr. Montague Boyd (1921), 563 Capitol Avenue, S. W., Atlanta.
Dr. William F. Braasch (1913), Mayo Clinic, Rochester, Minn.
Dr. Henry G. Bugbee (1916), 2 East 54th Street, New York.
Dr. Hermon C. Bumpus (1923), 110 North Madison Ave., Pasadena, Calif.
Dr. C. E. Burford (1926), 958 Arcade Building, St. Louis.
Dr. J. E. Burns (1922), 1210 Professional Building, Kansas City, Mo.
Dr. John R. Caulk (1912), 723 University Club Building, St. Louis.
Dr. Arthur B. Cecil (1921), 1016 Pacific Mutual Building, Los Angeles.
Dr. Fletcher H. Colby (1931), 205 Beacon Street, Boston.
Dr. J. A. C. Colston (1921), Johns Hopkins Hospital, Baltimore.
Dr. E. G. Crabtree (1924), 99 Commonwealth Avenue, Boston.
Dr. John L. Crenshaw (1924), Mayo Clinic, Rochester, Minn.
Dr. Arthur H. Crosbie (1916), 520 Commonwealth Avenue, Boston.
Dr. Harry Culver (1924), 7 West Madison Street, Chicago.
Dr. John H. Cunningham (1906), 46 Gloucester Street, Boston.
Dr. Edwin Davis (1922), 1436 Medical Arts Building, Omaha.
Dr. Clyde L. Deming (1928), New Haven Hospital, New Haven, Conn.
Dr. F. C. Edgerton (1906), 570 Park Avenue, New York.
Dr. W. A. Frontz* (1920), Johns Hopkins Hospital, Baltimore.
Dr. H. G. Fuller (1920), 209 Columbia Medical Bldg., Washington, D. C.
Dr. Joseph F. Geisinger (1933), Stuart Circle Hospital, Richmond, Va.
Dr. Roger C. Graves (1924), 12 Bay State Road, Boston.

*Deceased.

Dr. B. H. Hager (1930), 1136 West 6th Street, Los Angeles.
Dr. Homer G. Hamer (1923), 1711 N. Capitol Avenue, Indianapolis.
Dr. Leon Herman (1933), 801 Medical Arts Building, Philadelphia.
Dr. Charles C. Higgins (1933), 2050 East 93rd Street, Cleveland.
Dr. Frank Hinman (1920), 384 Post Street, San Francisco.
Dr. Joseph Hume (1921), 1107 American Bank Building, New Orleans.
Dr. Howard Jeck (1928), 745 Fifth Avenue, New York.
Dr. Herman L. Kretschmer (1916), 122 South Michigan Blvd., Chicago.
Dr. Thomas F. Laurie (1922), Medical Arts Building, Syracuse.
Dr. George R. Livermore (1922), 815 Medical Arts Building, Memphis.
Dr. David W. MacKenzie (1920), 305 Medical Arts Building, Montreal.
Dr. Charles M. McKenna (1916), 25 East Washington Street, Chicago.
Dr. Henry O. Mertz (1930), 1711 N. Capitol Avenue, Indianapolis.
Dr. J. H. Neff (1929), University of Virginia, University, Va.
Dr. Vincent J. O'Conor (1926), 55 East Washington Street, Chicago.
Dr. A. H. Paine (1922), 810 Medical Arts Building, Rochester, N. Y.
Dr. Frank S. Patch (1923), 1225 Bishop Street, Montreal.
Dr. William C. Quinby (1916), Peter Bent Brigham Hospital, Boston.
Dr. Alexander Randall (1920), 1323 Medical Arts Building, Philadelphia.
Dr. Nathaniel P. Rathbun (1921), 80 Hanson Place, Brooklyn, N. Y.
Dr. A. J. Scholl (1926), 523 West 6th Street, Los Angeles.
Dr. Thomas P. Shupe (1921), The Hanna Building, Cleveland.
Dr. Ira Sisk (1929), University of Wisconsin, Madison.
Dr. George G. Smith (1916), 6 Commonwealth Avenue, Boston.
Dr. Thomas C. Stellwagen (1932), 220 South 16th Street, Philadelphia.
Dr. Alexander R. Stevens (1916), 65 East 66th Street, New York.
Dr. William E. Stevens (1930), 870 Market Street, San Francisco.
Dr. Gilbert J. Thomas (1923), 1009 Nicollet Avenue, Minneapolis.
Dr. George W. Warren* (1915), 117 East 62nd St., New York.
Dr. Miley B. Wesson (1932), 490 Post Street, San Francisco.

*Deceased

CONTENTS

FIRST DAY

May 14, 1934

1. Calculus Replacement of the Prostate. J. Bayard Clark 1
2. The Evaluation of Resection of the Prostate. George R. Livermore 7
3. A Further Report on the Hormonic Control of Prostatic Function. William E. Lower, D. Roy McCullagh and Eugene L. Walsh 15
4. New Methods of Dealing with Difficult Strictures of the Prostato-membranous Urethra. Hugh H. Young 19

Discussion

5. Drainage Problems in Urology. N. P. Rathbun 47
6. Treatment of Tuberculosis of the Urinary Bladder. Gilbert J. Thomas, Thomas J. Kinsella, and Charlotte C. Van Winkle 55
7. Cystoscopic Technic Necessary for the Diagnosis of Genito-urinary Tuberculosis. Gilbert J. Thomas, Thomas J. Kinsella, and Charlotte C. Van Winkle 65

Discussion

8. State of Unilateral Anuria in Bladder Malignancy. Alexander Randall 77
9. Metastasis in Epithelioma of the Urinary Bladder. A. Dwight Spooner 81

Discussion

10. Treatment of the Atonic Bladder. William F. Braasch and Gershom J. Thompson 99
11. Late Results in Panmural Fibrosis of the Bladder. John L. Crenshaw 109
12. Incontinence of Vesical and Renal Origin (Relaxed Urethra and a Vaginal Ectopic Ureter). Miley B. Wesson 119

Discussion

SECOND DAY

May 15, 1934

13. Suppurating Polycystic Kidney. Joseph F. Geisinger 133
14. Tumors of the Adrenal Gland. Harry Culver and Marshall Davison 139
15. Paraganglioma of the Suprarenal Gland. Charles Morgan McKenna and Laurence E. Hines 151

Discussion

16. Tumors of the Renal Pelvis. Thomas P. Shupe 161
17. Papillary Carcinoma of the Renal Pelvis with Metastasis in the Ureter and Bladder. Robert C. Bryan 177

Discussion

18. Hyperparathyroidism and Renal Disease. Fuller Albright and Esther Bloomberg 195
19. Some Newer Conceptions of Urinary Stone Formation. J. Dellinger Barney and E. Ross Mintz 203

20. Anuria as a Complication of Lithiasis. J. Swift Joly 209
Discussion
21. Urine Formation in the Amphibian Kidney. A. N. Richards 241
Discussion
22. Resection of the Kidney. Herman L. Kretschmer 249

THIRD DAY

May 16, 1934

23. Transuretero-ureteral Anastomosis. Charles C. Higgins 279
24. Operative Injuries of the Ureter. Ira R. Sisk 287
25. Ectopic Vaginal Ureter. Clyde L. Deming 297
Discussion
26. Empyema of the Ureter Associated with Aplasia of the Kidney. George Gilbert Smith 321
27. Ureteral Occlusion Following Radium Implantation into the Cervix. Henry G. Bugbee 329
28. Calcified Tuberculous Mesenteric Lymph Nodes. Arthur H. Paine 339
Discussion
29. External Perineal Urethrotomy with Invagination and Resection of an Impermeable Stricture of the Penile Urethra. John R. Caulk 351
Discussion
30. The Gonadotropic Hormone in the Urine of Men with Tumor of the Testis. Frank Hinman and Tracy O. Powell 359
31. The Prognosis and Treatment of Tumors of the Testis. Frank Hinman 379
Discussion
32. Malignant Growths in the Undescended Testis. David W. MacKenzie 399
33. Nupercain as a Spinal Anesthetic. Howard S. Jeck 411
34. The Treatment of Malignant Disease of the Penis. Roger C. Graves 421
Discussion
President's Remarks 437

THE AMERICAN ASSOCIATION OF GENITO-URINARY SURGEONS

FIRST DAY, MAY 14, 1934

CALCULUS REPLACEMENT OF THE PROSTATE

REPORT OF A CASE

J. BAYARD CLARK, M.D.

New York City

This patient, aged fifty, white, married, a painter by trade, came to my service at the City Hospital, New York, in November, 1933. His family history was unimportant. His past history contained several incidents that may or may not be of significance. When eleven, while out in a boat, he was denied the opportunity to empty his bladder. This was followed by a temporary retention and later difficult evacuation. When nineteen, hemorrhoids began to trouble him. When twenty-three, he suffered from urethritis, probably non-specific. From then on he had an uneventful record until the age of forty-seven, when he began to have burning frequency and some difficulty at times in urinating. A show of blood sent him to a doctor who treated him for about two years. Failing to recover, he went to another doctor, who examined him by rectum and told him he had cancer of the prostate. This brought him to the City Hospital, where, upon our preliminary examination per rectum, we very nearly fell into the same error of diagnosis, that is, carcinoma of the prostate.

His chief complaints upon admission were difficult and painful urination and troublesome hemorrhoids.

He stated that his sexual life had been normal and active up to two months previous to entering the hospital.

The routine general physical examination revealed nothing of interest beyond the marked hemorrhoidal condition. The blood chemistry and blood Wassermann tests were negative. The urine examination was negative except for a few white blood cells. The urogenital examination revealed no evident pathology of upper urinary tract or external genitals. By rectal palpation one was given the impression of a large, fixed, stony-hard, fairly smooth prostate about the size of a hen's egg lying transversely, slightly sulcated down the center. The urine was clear. There was less than an ounce of residual urine.

The cystoscope passed easily. The bladder was trabeculated. The vesical sphincter was slightly irregular, lumpy. There was a rounded elevation of the floor just inside the vesical orifice but the ureteric ostia were normal and readily catheterized beyond the further slope of this elevation. Urethroscopy revealed what appeared to be a diverticulum to the left of the verumontanum.

Fig. 1. Flat plate.

Fig. 2. Cystogram—lateral view.

Up to this point a satisfactory diagnosis had eluded us, when the x-ray very dramatically solved the problem. A flat plate showed a large ovoid shadow. Cystograms demonstrated its exact position.

Being convinced that we had to do with a calculus formation of unusual size and wholly within the prostatic capsule, the subject of surgical approach became the next consideration. Two routes seemed possible—either transvesical or perineal. The perineal was chosen because it offered the surety of perfect drainage, though perhaps some difficulty in the matter of enucleation.

Spinal anesthesia was used. While the sound was being introduced as a guide it grated against the stone in its passage through the prostatic urethra. This was surprising, as two cystoscopies had been done

Fig. 3. Cystogram—front view.

without such contact. I shall refer later to this unsuspected communication with the calculus.

The usual incision and dissection as for perineal prostatectomy was made, and the prostatic capsule exposed. An incision three-fourths of an inch long was made a little off the median line to the left. I came directly upon the stone through an envelope hardly thicker than blotting paper. To my joy the stone was in two main segments and with a little rotating these parts were quite easily brought through the capsular cut. The examining finger within the capsule discovered no prostatic remains.

A drainage catheter was passed through the urethra to the bladder. No attempt was made to close the small opening of communication in the prostatic urethra previously discovered by the sound, as this, it was felt, would act as a useful means of drainage and close by itself, which it did. The capsule was lightly packed with a vaseline gauze drain and the structures brought together and closed.

The patient's condition seemed to be entirely undisturbed by the operation and the postoperative course and healing were uneventful. On the fifteenth day the perineal sinus had closed and he was comfortably passing all his urine by way of the urethra. When he left the hospital about a week later he was passing a good stream of good force and no residuum.

A letter from the patient three months after the operation stated that his sexual ability had returned, but that his hemorrhoids were

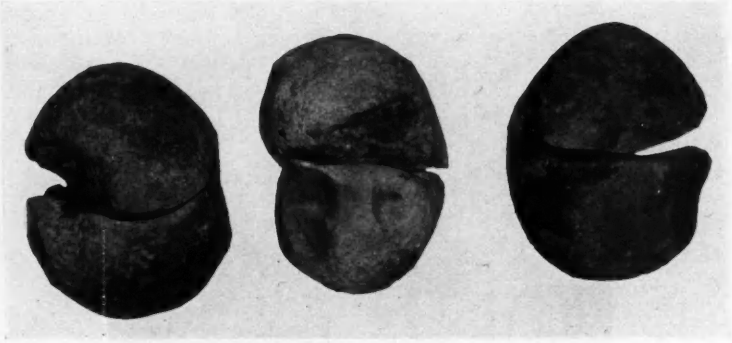


Fig. 4. Specimen viewed as a whole.

no better; that he still had some numbness of his legs but that he had gained twelve pounds in weight.

Pathologist's report of the specimen: Traces of iron and ammonia, large amounts of calcium, magnesium, carbonate and phosphate. Weight 58.5 grams. Size: 1 x 4.2 by 5.2 cm.

Aside from the unusual size of this formation and the interest it excites on that account, one is led to wonder if in such cases the stones can properly be classed as true prostatic calculi. Young,[10] in his Practice of Urology, states:

"Although prostatic and seminal calculi are not urinary calculi . . . they arise by deposition from the secretions present in the ducts just as urinary calculi arise from urine. The laws of their formation are undoubtedly the same. They are usually composed of cholesterin."

Kretschmer[4] is more explicit. In an article published in 1918, he says:

"Primary prostatic calculi have their origin within the prostatic tissue. They consist in the main of phosphates, carbonates or oxalates of lime, or magnesia or triple phosphates.

"Secondary prostatic calculi can be differentiated from the primary

by their chemical composition, the nucleus in these cases being composed of urates and earthy phosphates. The difference between the primary and secondary calculi must rest upon the chemical examination of the nucleus, for in this way only is one able definitely to determine whether one is dealing with a primary or a secondary stone.

"Secondary stones may have an outer coating of the same composition as the true calculi. Hence the importance of determination of this point: namely to have the center of the stone subjected to careful chemical examination."

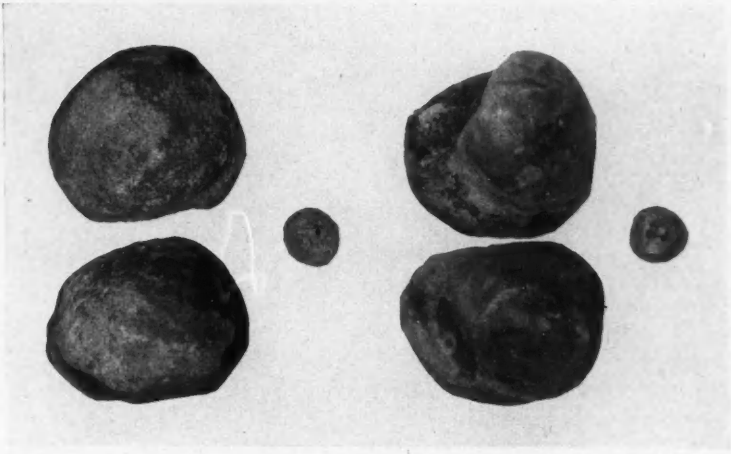


Fig. 5. Specimen disarticulated.

According to Kretschmer this case might be said to belong to his classification of primary prostatic calculi in that the stones unquestionably had their origin within the prostatic tissue and consisted of those elements properly belonging to true prostatic calculi. Yet in cases of very large concretions such as mine, it is difficult to imagine these concretions attaining their unusual size from the outpouring of prostatic secretions alone; especially is it difficult to imagine when they have practically obliterated from their mere preponderance all, or practically all, of the tissues from which they are nourished. It would seem, therefore, that in such cases the stones had access to a more generous supply of that which gives them substance, and that supply could be drawn from no other source than the continuous wash of the urinary stream.

In this case it has been shown that there was an opening through the prostatic urethra accidentally discovered by the sound introduced as an operative guide, and that in the urethroscopic examination there was seen what was taken to be the window of a diverticulum. It will be remembered also that this patient in his early youth had an unusual strain put upon the integrity of his lower

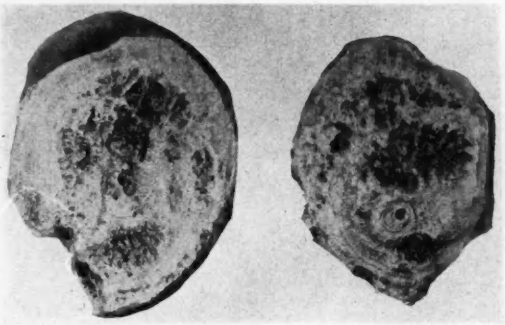


Fig. 6. Interior view of calculus.

urinary tract when he was denied the opportunity to evacuate a painfully distended bladder. Whether this incident has any etiologic bearing upon the case it is impossible to say, but at least we should bear in mind the possibility of a communication with the urinary passages when we encounter large prostatic calculi which have all the casual appearances of true prostatic calculi.

REFERENCES

1. GIANNUZZI, ARMANDO: Grosso Calculo Prostatico Vero. Arch. ital di chir., 18:478, 1927.
2. HUBERRY, N. L.: Am. Jour. Roentgenol., 6:286-289, 1919.
3. JUDD and CRENSHAW: Prostatic calculi. Minn. Med., 2:52-56, 1919.
4. KRETSCHMER, H. L.: True prostatic calculi. Surg., Gyn. & Obst., 26:70-76, (January) 1918.
5. KRETSCHMER, H L.: True prostatic calculi. Surg., Gyn. and Obst., :163-168, (February) 1927.
6. LYDSON, G. FRANK: A case of enormous prostatic calculi. Ann. Surg., 39:391, 1904.
7. MCGWAN, J. P.: A case of large prostatic calculus. Trans. N. Y. Soc-of Derm. & G. U. Surg., 1908.
8. NICOLICH: Enorme Calcul de la Prostate. LAssoc. franc. durol., 13:70-76, 1909.
9. STETTEN, DEWITT: Calculus cast of prostate. Am. Surg., (March) 1923.
10. YOUNG, HUGH H.: Practice of Urology.

THE EVALUATION OF RESECTION OF THE PROSTATE

WITH REPORT OF CASES

GEORGE R. LIVERMORE, M.D.
Memphis, Tennessee

The value of prostatic resection has already been proved by Davis, McCarthy, Alcock, Caulk, Bumpus, Kerwin, Day, Livermore, Kretschmer, Boyd, Moore, Folsom, and others. It only remains for us to check over our work, note its deficiencies, see wherein the patient's morbidity may be lessened, his complications and mortality reduced, and his ultimate and complete recovery hastened.

We all know that there must be some mortality following resections, but that it is a simple procedure devoid of danger and never resulting in death is a statement that all of us know is not true. In looking back over my cases since I began this work I see many perfect cures, a few that were not so perfect, and a mortality rate that is far better than most of us obtained with prostatectomy. As we have become more proficient in its performance, we have felt more certain of our results, and our mortality in the first 100 cases is 4 per cent.

We urologists know the dangers that beset patients with obstructive lesions at the bladder neck; the many complications to which they may fall heir, and the vicissitudes to which they may be subjected from hemorrhage, infection and cardio-vascular renal insufficiency. It is needless for me to dwell upon this aspect, because you are too familiar with the reactions that follow the introduction of a catheter or a sound, not to appreciate fully the greater danger following the removal of the obstructing prostatic tissue, and the denudation of the internal meatus and prostatic urethra. The burned and dehydrated area must necessarily slough, thus furnishing infection with a splendid culture medium and the denuded areas are open doors which may lead to widespread dissemination. We, therefore, appreciate the fact that it is a highly technical procedure, requiring the greatest precision and skill, and with a mortality of from 4 to 6 per cent.

Many patients have a high resistance and withstand almost any

amount of punishment to the urethra and bladder without great reaction; while others, regardless of preparation, urinary antiseptics, vaccines, foreign proteins, or what not, develop the most violent reactions which may result in lung, heart, or kidney complications that carry the patient off, regardless of anything we may do.

A certain group, just as after prostatectomy, will stand the operation well, but instead of gradually improving, and advancing to complete recovery, will continue to decline, resisting all our efforts, without any definite evidence of the cause of the decline, and pass away. Hemorrhage, infection, pneumonia, uremia and embolism were the chief causes of death in prostatectomy. All may occur after resection, but not as frequently as after prostatectomy. The sooner these facts are realized and frankly stated, the better it will be for us, and the easier for the patient's family, who will be spared the shock of an unexpected death.

Preparation of the patient: I am as careful in preparing patients for resection as I am for prostatectomy. The same painstaking check-up of the cardio-vascular renal system is made, the same coördination of renal function and blood chemistry, and the same complete physical examination that insures the best possible operative condition. All patients are decompressed, regardless of the amount of residual urine, and every one is kept on catheter or suprapubic drainage for, at least, one week prior to resection. Fluids are forced. Hexamethylenamine tetramine grs. 10, and tincture of belladonna m. 10, are given four times a day, and salol grs. 5, three times a day. If the urine is not acid, ammonium chloride, or acid sodium phosphate grs. 10, is administered three times a day. Should the patient have fever, and this is not rare, under catheter drainage, hexamethylenamine tetramine grs. 31 is given intravenously twice a day. A low protein diet (with green vegetables and fresh fruits, especially oranges) is another requisite. The patient should be kept out of bed and have an abundant supply of fresh air and sunshine.

He is not told when he is to have his operation, and if restless the night before, he is given bromide, trional, or both to insure adequate rest. He is urged to drink water freely until two hours before operation, when he is given sodium amytal, grs. 3, by mouth, and one hour later, morphine gr. ¼, and hyoscine, gr. 1/100, are

given hypodermically. If he is not asleep in one-half hour, another ⅛ gr. of morphine is administered. A few patients may be talkative, or restless, but if another ⅛ gr. of morphine is given, they usually drop off to sleep.

An enema is given two hours before operation, and one hour later 8 ounces of glucose and soda solution are introduced per rectum and the foot of the bed elevated 6 inches. After such preparation the patient comes to the operating room in profound sleep, or so drowsy he is roused with difficulty. Sacral anesthesia, 10 c.c. of 3 per cent novocain is injected into the canal, and about 2 c.c. of 1 per cent into each sacral foramen. The McCarthy resectoscope is introduced, and the internal meatus and prostatic urethra are carefully inspected. I usually begin to resect the lower aspect of the internal meatus, and then pass forward into the prostatic urethra, and resect the intra-urethral lobes. After this, the lateral aspect and the roof of the internal meatus are dealt with. It is remarkable how the resection of one portion of the obstructing prostate will often cause obstruction in another, and it is a fact that when we feel that one or two more cuts will complete the operation, these one or two cuts cause the projection of more nodules, that require considerably more resection before our task is ended.

It has been my experience that the McCarthy sheath often holds the prostatic urethra so widely open, projections of obstructing prostate may be overlooked. It is, therefore, my custom when I think I have a good channel, to remove the McCarthy scope and introduce the panendoscope, to make sure that all obstructions have been removed.

It is surprising how often nodules have been overlooked. Especially is this true of projections in the prostatic urethra. Hemorrhage is a much mooted question. Many men dismiss it with a few words, in fact, too few, for it is one of the most important factors in the success of the operation. Severe hemorrhage is rare. I am sure I can count on the fingers of one hand the cases in which hemorrhage of any great magnitude has occurred. On the other hand, the cases in which it has been annoying (almost a constant clouding of the field that made vision difficult, stopping when the coagulating current was applied, only to recur when the resectoscope was moved), cases too in which much more time is spent in

controlling hemorrhage than in resecting the prostate, are not uncommon.

In several cases severe hemorrhage that required ten minutes to control has been encountered and in two cases, despite the introduction of the McCarthy panendoscope, and a large bulb electrode, the hemorrhage continued practically unabated; the especially mystifying part being that with the panendoscope in the bladder and the entire field carefully explored, no bleeding point could be seen by me, or my associate, Dr. Turley, and on removal of the scope, excessive hemorrhage returned. This is probably accounted for by the pressure of the instrument.

In both cases we were able to control the hemorrhage finally with the coagulating current, and by pressure on the prostate per rectum against the panendoscope in the prostatic urethra. Both patients, when returned to their rooms, had bloody drainage, but under hot saline irrigation, no clots were allowed to block the catheter and both had only a wine colored drainage by afternoon.

In two other cases hemorrhage was so severe after each cut, the time consumed and the loss of blood were so great before the bleeding was controlled, that I discontinued the resection and finished it ten days later with very little and easily controlled hemorrhage. Secondary hemorrhage has occurred in three cases; one on the sixth day, one on the twelfth day, and one on the day of operation. In one it was controlled by the re-introduction of the retention catheter, and the injection of 1 per cent nitrate of silver solution. In the second case the patient had gone home to a town about 200 miles from Memphis when it occurred. His local physician telephoned and asked what to do. He was told to replace the catheter and leave it in forty-eight hours, and irrigate with hot saline solution. This was done and all hemorrhage promptly stopped. The catheter was left in for twenty-four hours, and then removed. Hemorrhage promptly returned and the physician again telephoned me, asking what to do. He was again told to replace the catheter and send the patient back to me. He was unable to introduce the catheter, and as the bladder filled quickly with blood and clots, the patient was so uncomfortable he performed a suprapubic cystotomy, and after emptying the bladder and instituting suprapubic drainage the hemorrhage promptly ceased.

In the third case, a ward patient with no special nurse, the catheter was allowed to become occluded with a clot, and when I

saw him one and one-half hours after operation the catheter could not be opened. He was returned to the operating room, the bleeding vessel fulgurated, and the hemorrhage controlled. Although his tests were all right he was a frail man, and the loss of blood necessitated a transfusion. As he did not gain as he should, a second and third transfusion were given in the next few days. Nausea and vomiting were frequent, so a Levine tube was introduced, but despite large quantities of fluid and nourishment through it, and glucose and saline solution given intravenously and by hypodermoclysis, he continued to fail, and died on the tenth day after operation.

I have recently heard of a case of secondary hemorrhage that occurred three weeks after operation and, despite its control and transfusion, the patient died. He was resected by another Memphis urologist, who reported the case to me.

When the operation is completed a 26 F. retention catheter is introduced, and if there is no active hemorrhage, the patient is returned to his room. Constant supervision by a well trained nurse is imperative to prevent occlusion of the catheter by clots. Should it occur, the injection of hot saline solution quickly frees it, and even though the drainage may be quite bloody, if kept flowing, the bleeding usually ceases. If it does not, we inject hot water to wash out the saline solution, then inject 1 ounce of 1 per cent nitrate of silver and clamp the catheter for five minutes. If this does not control it, the injection of hot water, followed later by hot saline solution, usually does so. If this fails, the index finger is introduced into the rectum, and the prostate is pressed against the catheter in the prostatic urethra. If this fails, reintroduce the resector and fulgurate the bleeding vessel. Uritone, grs. 31, is given intravenously before the patient leaves the operating room and twice daily for a week, or longer, if the patient has rigors or fever. Urotropin given intravenously is not a "cure-all," but it certainly prevents reactions in the great majority of cases, and in those in whom reaction occurs it reduces their severity. I am sure you are overlooking a wonderful aid if you are not giving your patients the benefit of its use. Five hundred c.c. of 5 per cent glucose solution in saline are given intravenously or by hypodermoclysis when the patient returns to his room. Caffeine sodio benzoate grs. 3, and digifolin 1 c.c. by hypo., every five hours, prn., as heart and kidney stimulants, and pantopon gr. ⅓ prn., for pain.

The 26 F. catheter is removed on the fourth day. Incontinence has occurred quite frequently in my series, but fortunately is only temporary and clears up after the denuded area has healed. If not, a few dilations of the prostatic urethra and internal meatus usually bring about complete control. In those cases in which it

STATISTICS ON 100 CASES OF PROSTATIC RESECTION

	No. Cases	Per Cent
Mortality	4	4
1. Pulmonary Embolism (Age 61)		
2. Myocarditis (Age 67)		
3. Myocarditis (Age 76)		
4. Uremia (Age 66)		
Complications		
Epididymitis	15	15
Uremia	4	4
Incontinence	5	5 (all temporary)
Hemorrhage		
Primary	3	3
Secondary	3	3
Shock	2	2
Carcinoma	8	8
Vesical Calculi	3	3
Anesthesia		
Sacral, Morphine		
Hyoscine and Sodium Amytal	98 (4 deaths)	4.08
Spinal and Synergistic	2 (no deaths)	2

Reactions: Ten patients had rigors and temperature above 103, four had several rigors and temperature 102 to 104. All others had some fever, usually for only one or two days, never above 102, but no rigors. Uritone gr. 31 was given intravenously twice a day.

does not, there is some irregularity; a tag, or nodule left in the internal meatus, or prostatic urethra. The application of the McCarthy cutting current, or Collings' electrotome, which may have to be repeated, will cause enough sloughing to bring about complete control, unless there is contracture of the external meatus, or a stricture. For the former a meatotomy must be done, and for the latter dilation to bring about relief.

Epididymitis has occurred in about 20 per cent of my cases. In some it may develop in the first three or four days after operation, though it usually makes its appearance after the catheter has been removed, and sometimes does not occur until the patient is up and about two or three weeks after the operation. In view of the fre-

quency of epididymitis, I think it advisable to do a vasotomy and ligation prior to resection in those patients who are not good risks, and in those who are more or less melancholy, for when epididymitis occurs in such cases, it may prove the last straw that breaks the camel's back.

David M. Davis' method of ligating the vas is so simple and so quickly done, I have ligated the vasa routinely since the publication of his method. I am a firm believer in the benefit of large amounts of water in these cases. We make it a rule to give saline solution, or glucose 5 per cent, at least, 500 c.c., once or twice for the first twenty-four or forty-eight hours, and more if the patient shows any need for it. He is carefully watched for any symptoms of acidosis or alkalosis. In both conditions the urine output is diminished, and hence uremic symptoms will soon develop if this is not corrected. Glucose and alkalies in the former, and sodium chloride in the latter, usually bring about relief. A dosage of 50 to 100 c.c. of 10 to 25 per cent sodium chloride given intravenously not only supplies chloride which aids biochemical changes that permit extraction of water from the tissues, but also acts as a laxative, thus aiding the kidneys in eliminating waste products from the system.

The evaluation of prostatic resection may be summed up as follows:

1. Value in the relief of obstruction. The satisfactory results in resection for relief of obstruction, as testified by both patients and surgeons, speak for themselves.

2. Value in the reduction of morbidity. This is adequately proved by the diminished suffering and the marked shortening of hospitalization, average seven to eight days.

3. Value in the reduction of complications. Except in cases of epididymitis, the value of resection is too well established to need any proof, and now that we have David M. Davis' method† of vas ligation this, too, will be eliminated. Open operation, with severing and ligation, is best.

4. Value in the reduction of mortality. Here, also, resection has no need for a champion as we know full well that the mortality for prostectomy of all operators was from 40 to 50 per cent, whereas even with the statistics of Alcock, many of whose cases were human derelicts, the mortality of resection has never exceeded 25 per cent and now is well below 5 per cent.

†Trans. Southwestern Branch A. U. A., 1933.

A FURTHER REPORT ON THE HORMONIC CONTROL OF PROSTATIC FUNCTION

WILLIAM E. LOWER, M.D., and (by invitation) D. ROY McCULLAGH, M.D., and EUGENE L. WALSH, M.D.

From the Cleveland Clinic, Cleveland, Ohio

Numerous investigators have demonstrated the existence of androtin, the male sex hormone which is soluble in lipoids and lipoid solvents, and they have shown that it probably is derived from the interstitial cells of the testis under the influence of the gonad-stimulating hormones of the anterior lobe of the pituitary gland. This hormone, androtin, may be recovered from the urine of normal males. Accumulating evidence seems to indicate that androtin is not the sole autacoid of the testis. It alone fails to explain all of the endocrinologic functions of the testis.

If two animals be united surgically with their peritoneal cavities in free communication, various hormonic interchanges occur in the peritoneal fluids. This technic, producing surgical pseudo-Siamese twins, is called parabiosis. Two normal animals survive such a procedure with no disturbance of function. However, if one partner is castrated, his pituitary gland becomes hypertrophic and produces an excess of gonad-stimulating secretion, which apparently reaches the normal partner by way of peritoneal transfer. The effect of this on the testes of the uncastrated rat is added to that of his own normal pituitary secretions. This, in turn, results in a marked gross and histologic hypertrophy of the prostate and seminal vesicles within a period of twenty days. The castrated partner has a marked prostatic atrophy due to the lack of the oil-soluble male sex hormone which presumably can not pass in any appreciable amount from the normal to the castrate through the peritoneal fluids (Fig. 1). This method offers a way of producing a true physiologic hypertrophy of the prostate in a rat.

By injecting rat testicular mush into the castrated partner of a normal-castrate parabiotic union, the hypertrophy of the secondary sex glands which occurs in untreated parabiotic animals can be prevented. In some animals, the prostate is reduced to even less than normal size (Fig. 2). Martins and Rocha[2] have obtained somewhat similar results. We have shown further that injections of

juice expressed from bulls' testicles has a like effect. This is due, theoretically, to an inhibition of pituitary function in the castrated partner by the expressate from testes.

Because of these experiments and others which will be described in detail in a later publication, the presence in the testis of an hypo-

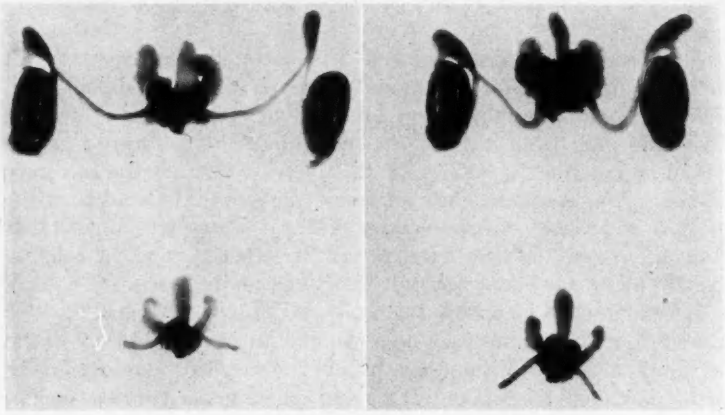


Fig. 1 *(left)*. Hypertrophied secondary sex glands in the normal partner of an untreated normal-castrate parabiotic pair; atrophy of prostate in castrated partner.

Fig. 2 *(right)*. Sex glands from a normal-castrate parabiotic pair of animals after treatment of the castrate with testes mush. Note that the hypertrophy of the secondary sex glands in the normal partner has been prevented.

thetical water-soluble chalone,* inhibin, has been postulated.[1] One function of this may be inhibition of pituitary activity.

Inhibin is a purely theoretical substance, but the evidence of its existence is sufficiently suggestive to warrant further study. This is especially true in view of an interesting hypothetical theory of etiology of prostatic hypertrophy, which we have stated previously. This postulates that the testis secretes a substance which inhibits overactivity of the pituitary gland. In senescent men, degenerative changes in the germinal epithelium and a retardation of spermatogenesis indicate diminished functional activity. At the same time, there is a decrease of pituitary-inhibiting secretion. The pituitary then becomes hyperfunctional and stimulates the interstitial cells

*We prefer to use Schäfer's classification of internal secretions, all being classed generally as autacoids. Hormones are those stimulatory in nature; chalones, those which inhibit.

of the gonads to elaborate an excess of male sex hormone, resulting in prostatic hypertrophy.

This tentative theory is purely hypothetical, but because of its possible clinical application, should it be correct, we decided to determine whether or not any direct attack might be made either to prove or disprove the existence of the testicular chalone, inhibin.

Normal rats have received daily injections of the juice expressed from bulls' testes. Within a three-week experimental period this procedure results in a marked decrease in the size of the prostate and seminal vesicles. This decrease in size, atrophy of a fashion, is due theoretically to an inhibition of pituitary function. This effect might possibly be caused by nonspecific proteins, but this seems unlikely in view of the experiments to date. At present we are engaged in making various fractions of bull testis juice. All these experiments are indicative of the existence of inhibin but at present are not conclusive enough to warrant a positive statement regarding it.

SUMMARY

Experimental work on the endocrine functions of the testis indicates that male sex hormone, androtin, does not wholly explain various factors in testicular physiology. Injections of a water-soluble preparation from testes reduces the size of the prostate in experimental animals, exactly the opposite effect from that obtained by injections of androtin. Hence the existence of inhibin, a second autacoid of the testis, has been postulated. This is an hypothetical, water-soluble chalone, which inhibits pituitary activity. The experimental work indicates that such an autocoid exists and other experiments are under way to determine more definitely its nature and function.

REFERENCES

1. McCULLAGH, D. R.: Dual endocrine activity of the testes. Science, 76:19-20, (July 1) 1932.
2. MARTINS, T., and ROCHA, A.: The regulation of the hypophysis by the testicle, and some problems of sexual dynamics. Endocrinology, 15: 421-434, 1931.

NEW METHODS OF DEALING WITH DIFFICULT STRICTURES OF THE PROSTATO-MEMBRANOUS URETHRA

HUGH H. YOUNG, M.D.

From the James Buchanan Brady Urological Institute, Johns Hopkins Hospital, Baltimore

The technical care of strictured conditions in the deep urethra, resulting from traumatism, disease or operation, often presents a serious problem. I wish to bring before you some of the methods that I have employed to combat difficulties encountered. I shall first cite the difficulties experienced in a case of ruptured urethra.

Case 1.—J. M., male, aged forty-four years, was admitted September 3, 1931, for relief of impermeable stricture of the posterior urethra. Seven years previously a large generator had fallen upon the patient, and he had suffered a traumatic rupture of the urethra as a result of this blow. An immediate operation, supplying suprapubic drainage of the bladder, and perineal drainage of the prostatic region, was performed elsewhere. Many subsequent operations were done (elsewhere), in attempts to cure the impermeable stricture of the urethra that resulted.

On admission here, the patient had a permanent suprapubic drain. It was impossible to pass any instrument, and a long area of scar tissue, with complete obliteration of the urethra, was discovered at operation, after the excision of which it was possible to carry out an end-to-end anastomosis of the prostate to the membranous urethra. The immediate result was excellent, but after the patient returned home, he failed to secure periodic dilatation of the urethra.

After many months he returned with a very tight stricture of the urethra, through which urine was voided with great difficulty. Examination showed the apex of the prostate and membranous urethra surrounded by much fibrous tissue. In front of this the bulbous urethra was considerably dilated and pocketed, as a result of numerous attempts to pass instruments into the bladder. Catheters and sounds met with a very firm obstructive wall. Filiforms engaged in something, and may have entered a short distance into the membranous urethra (Fig. 1, No. 1), but buckled two or three times upon themselves.

Reviewing the case, it was evident that two conditions had to be dealt with: (1) the difficulty of engaging and penetrating the urethral lumen of the strictured area, owing to the irregularly dilated urethra

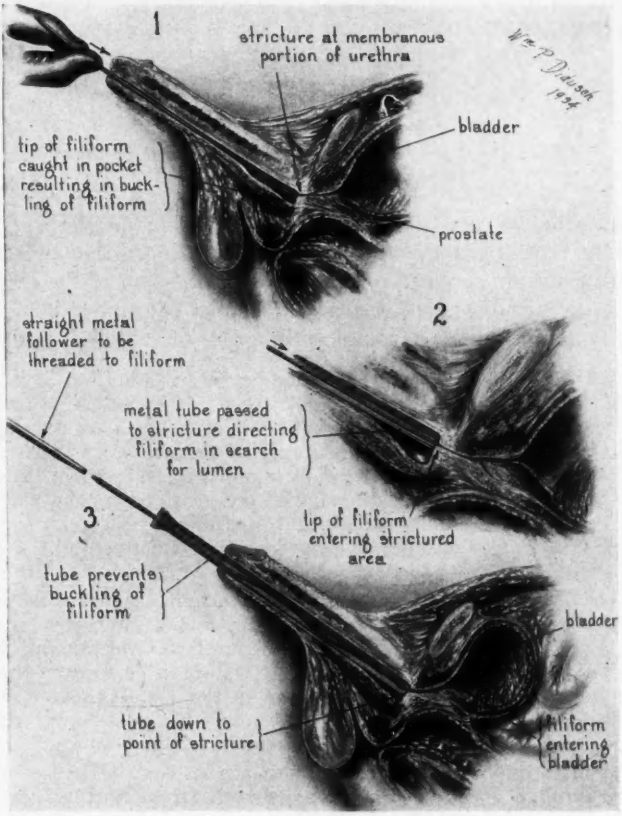

1
stricture at membranous portion of urethra
bladder
tip of filiform caught in pocket resulting in buckling of filiform
prostate
2
straight metal follower to be threaded to filiform
metal tube passed to stricture directing filiform in search for lumen
3
tip of filiform entering strictured area
tube prevents buckling of filiform
bladder
tube down to point of stricture
filiform entering bladder

Fig. 1. Case 1. No. 1. Conditions present in a case of pronounced stricture of the anterior, prostatic and membranous urethra after operation for rupture of the urethra. The urethral lumen in the strictured area was small and eccentric. The tip of the filiform engaged in a pouch near the floor of the urethra, and the filiform doubled upon itself, as shown. No. 2. Use of Young's urethral tube to assist the filiform in searching for the lumen of the urethra, which was finally engaged. No. 3. Use of urethral tube to prevent buckling of the filiform while the attached bougie is passed down the tube.

immediately in front of the strictured membranous portion; and (2) preventing the filiform from doubling upon itself.

To meet these conditions I had constructed in our shop a tube about one-quarter of an inch in diameter, which could be passed down into the bulbous portion of the urethra. Inserting a filiform into this I was able, by moving the outer portion of the tube (Fig. 1, No. 2), to bring the point of the filiform to various places in the indurated mass, in which lay the lumen of the membranous urethra. Finally, by depressing the outer portion, and thus searching the superior surface of the urethra, the lumen was engaged by the filiform (Fig. 1, No. 3), which, without much difficulty, passed through the prostatic urethra into the bladder. The small tube had effectively prevented the filiform doubling back upon itself. Removing the tube, I then

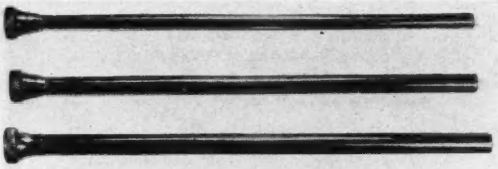


Fig. 2. Young's urethral tubes to guide filiforms through strictured lumina and prevent buckling of filiforms.

attached to the filiform a curved steel following sound (LeFort) and pushed it on into the urethra, but soon discovered that the filiform had again doubled upon itself, thus making it impossible to carry the sound through the strictured urethra. I then removed the follower, reinserted the tube, and attached to the filiform a flexible bougie follower (Fig. 1, No. 3), which was small enough to pass down the tube. No difficulty was then experienced in pushing this flexible bougie, led by the filiform, through the strictured area into the bladder. The tube had effectively prevented the filiform from buckling.

Having thus succeeded in introducing a No. 12 flexible follower bougie into the bladder, I had our mechanic make a series of tubes (Fig. 2). These varied from No. 16-F to 28-F in size. Thus equipped, a few days later I again attacked the stricture. Filiforms were first tried alone, but here again they doubled upon themselves, and it was impossible to determine whether they had actually entered the strictured urethra or simply engaged in some pouch or false passage in the bulbous urethra. By means of the small tube, which had previously been employed, the proper orifice was soon found, the filiform passed into the bladder, followed by a flexible bougie, which was withdrawn, unscrewed from the filiform, the tube removed, a

larger one inserted, and another bougie of greater caliber successfully passed through the strictured urethra into the bladder. Using this method at intervals of two to three days, it was soon possible to dilate the urethra up to about No. 20-F by means of flexible bougies. When a larger, flexible bougie was used, too great resistance was encountered to force it through the strictured area. Accordingly, I had made at our shop metal bougies, without a curve (Fig. 3). They were

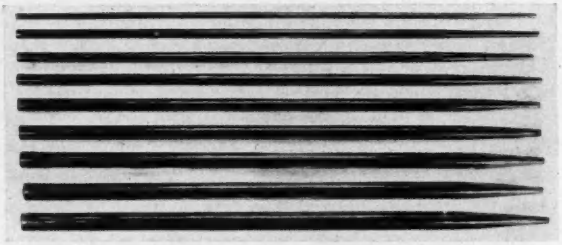


Fig. 3. Young's straight metal followers attachable to filiforms, and used with or without the urethral tubes to dilate difficult strictures of the anterior urethra, but also very bad strictures of the prostato-membranous urethra. These followers are now made with the outer end conical, without a screw hole for use without filiforms, particularly after hypospadias operations.

practically identical with the flexible bougies. One of these instruments, when attached to the filiform (Fig. 1, No. 3), easily passed down a urethral tube until the filiform had gone entirely through the bulbous urethra (Fig. 4, No. 2). The urethral tube was then removed, and the metal straight bougie carried through the strictured area into the bladder (Fig. 4, No. 3). The fact that it was straight seemed to make no difference, the filiform itself furnishing the necessary curve to lead it over the median portion of the prostate into the bladder. In the subsequent treatment of this case, these straight metal bougies were successfully used up to No. 26-F, and, although the fibrous mass in the perineum was very resistant, no great difficulty was encountered in pushing them on into the bladder. The filiform was in no case bent or broken. I am confident that the force employed was done with much greater safety than could have been used with the curved metal follower. The use of cystoscopes, urethroscopes and instruments for resection have taught us that it does not require much, if any curve, to go into the bladder. I have long been of the opinion that there was danger in the use of the markedly curved metal dilators, which we have employed in the past.

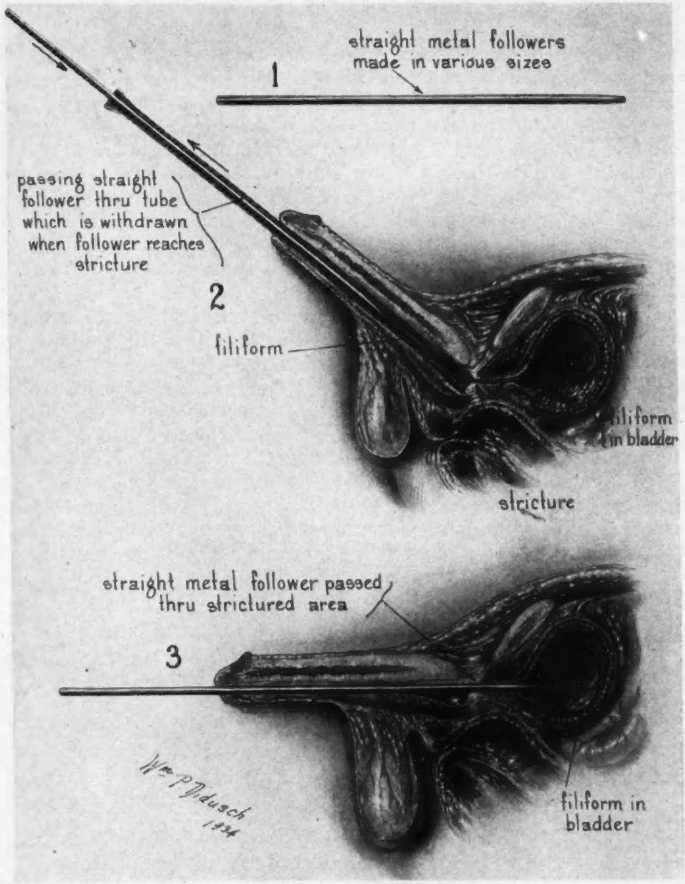


Fig. 4. Case 1. No. 1. Young's metal followers. No. 2. The metal tube is being used to prevent buckling of filiform, but is removed when the follower reaches the stricture, in order to facilitate the deeper passage of the follower. No. 3. Follower passed through stricture.

Owing to the roughened condition of the strictured area, and the greatly dilated bulbous urethra, it was never possible to do without the tubes, which were necessary to prevent the buckling of the delicate filiform.

Case 2. A severe stricture of the membranous urethra, which followed my double sphincter plastic operation to cure incontinence of urine, was present. Filiforms engaged, but would not pass, forming several doubles in the capacious bulbous urethra. During these manipulations, I thought at one time the filiform had gone well through into the bladder, and attached the steel dilating follower. I deceived myself into believing that the beak had entered the stricture correctly. But, as it would go no farther, I withdrew it, and found that the filiform had broken. Bleeding indicated that the urethra had been traumatized, producing a pouch, or small passage, as a result of the doubling of the filiform. After a few days I again used the urethral tubes shown in Figure 3. I had no difficulty in finally discovering the orifice through which the filiform passed easily into the bladder, supported as it was by the tube which prevented its doubling. Dilating bougies, which were attached to the filiform, were also passed in this case with increasingly large tubes to prevent doubling of the filiform, and little difficulty was experienced in bringing the urethra practically to normal size by the use of this technic. After a time the strictured urethra became so much softer that filiforms and ordinary metal followers could be employed, and ultimately sounds passed consecutively at intervals during the succeeding months. As a result of this treatment, it was possible eventually to dispense with dilatations, the patient had a normally functioning urethra, and was cured of his incontinence.

In such cases it is important not to proceed too rapidly. To cure these patients one must excise all except a small portion of mucosa in order to draw the periurethral muscle (sphincter) into tight contact after excising the scarred tissue (remaining after transurethral resection, or an improperly performed perineal or suprapubic prostatectomy). In other words, it is necessary to produce a stricture to cure the patient. This must be very cautiously dilated to avoid a rupture, which would impair the newly made sphincter.

The set of urethral tubes, above described, has been used successfully now in various types of cases, particularly those in which strictures were deep seated, eccentric, or surrounded by pockets in which filiforms would engage. Support given the delicate filiforms by the tubes effectively prevents doubling of the filiform, both during the passage through the stricture into the bladder, and subsequently while conducting a follower to the deep urethra and

through the sphincter. Judging by our experience, these tubes should prove a valuable addition to the armamentarium of stricture therapy.

THE USE OF THE CYSTOSCOPE TO PASS INSTRUMENTS RETROGRADE FROM THE BLADDER THROUGH STRICTURES OF THE PROSTATIC OR MEMBRANOUS URETHRA

In cases that have been subjected to operations upon the mem-

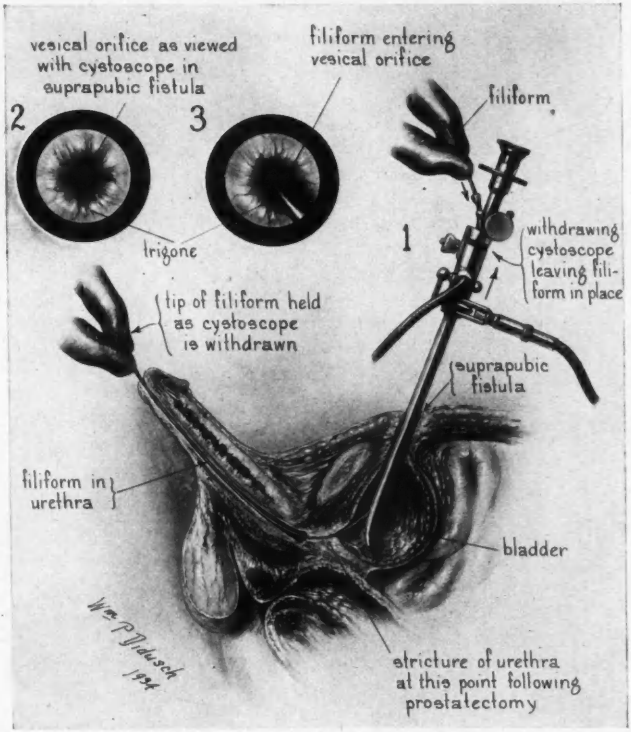


Fig. 5. Retrograde passage of filiform through catheterizing cystoscope passed into bladder through suprapubic fistula.

branous or prostatic urethra (operations for rupture of the urethra, double sphincter operations for incontinence, epispadias with incontinence, et cetera) before devising the urethral tubes above de-

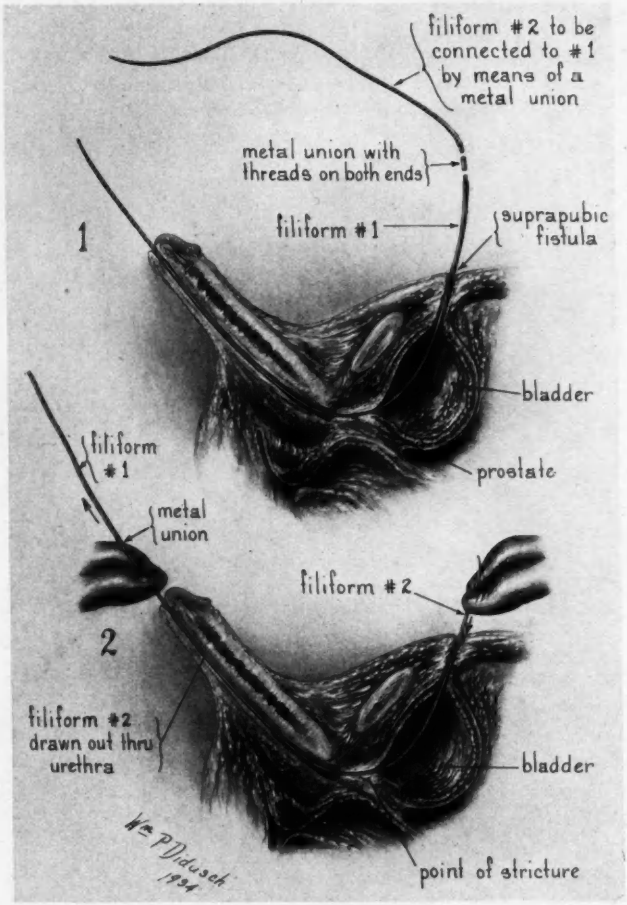


Fig. 6. No. 1. A second filiform is being attached to the one that has been introduced through the suprapubic fistula out through the urethra by means of a metal coupler. No. 2. The second filiform is drawn out through the fistula and urethra until the butt end appears at the meatus, when it is detached from the first filiform.

scribed, we occasionally made use of a cystoscope introduced through the suprapubic wound (Fig. 5, No. 1), to pass filiforms through the strictured urethra. In such a case I have usually employed a filiform with a ureter catheterizing cystoscope. After locating the urethral orifice (Fig. 5, No. 2) no difficulty was experienced in passing the filiform into the prostatic urethra (Fig. 5, No. 3) and in the majority of cases it would also pass retrograde on through the strictured area and out the meatus, where its point

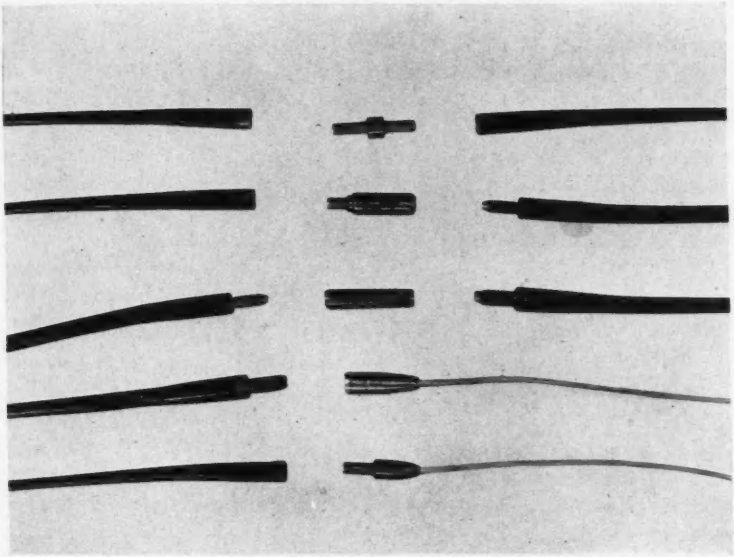


Fig. 7. Various filiforms and different types of couplers necessary to connect them. In two lower photographs, a coupler attaching a thread or silkworm gut to filiform is shown.

was caught by an assistant. Withdrawing the cystoscope, and catching the screw end, which projects a short distance from the suprapubic fistula, one was confronted then with the problem of passing dilating followers through the strictured area. By screwing a dilating bougie onto the filiform, and making traction upon it, the dilator was pulled and pushed through the suprapubic wound,

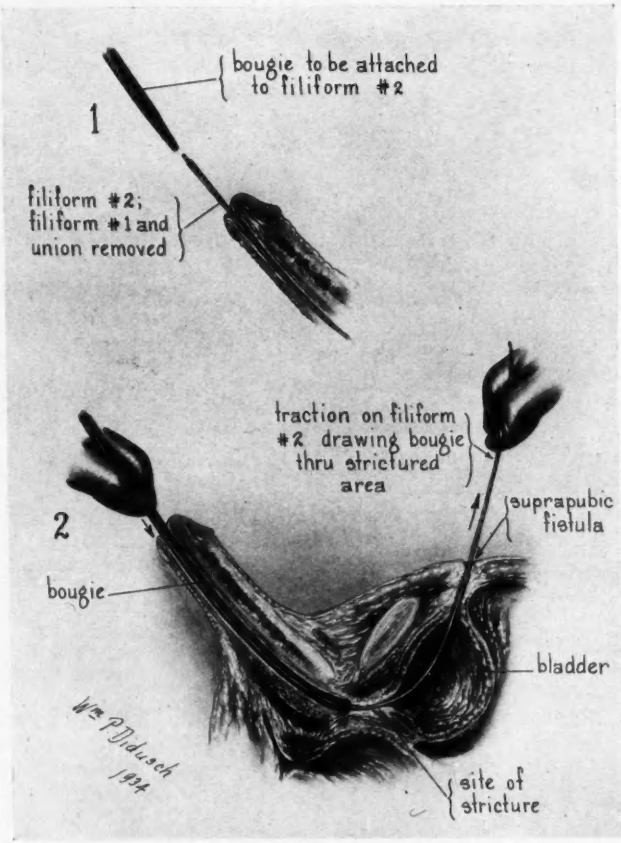


Fig. 8. No. 1. Flexible bougie is being attached to the second filiform, which has been drawn through the suprapubic fistula. No. 2. Method of passing the flexible bougie by combined traction and pushing.

and the strictured area out to the glandular meatus. No metal instrument could be used for this.

At other times retrograde passage of a dilating bougie is not satisfactory, as not enough pressure can be exerted upon the flexible bougie. It is then desirable to attach another filiform to the one passed retrograde, thus fastening the butt ends together (Fig. 6, No. 1) by means of a coupling tube, so that the second filiform can be drawn out until its screw end projects from the meatus. The operator is careful to hold on to the pointed end, so as to prevent its escaping into the bladder (Fig. 6, No. 2). Dilating followers are then attached to the filiform, and, by combined pushing and traction, are carried through the strictured area one after another until sufficient dilatation for that seance is accomplished. In our armamentarium are dilators which carry various types of filiforms (some male, some female, some with small threads and others with a large thread) so that in practice it has been found necessary to have screw couplers, with which every type of filiform can be attached to every other. Some of these combinations are depicted in Figures 7 and 8. With these simple screw couplers, no difficulty is experienced in passing filiforms and followers of various types through the urethra and out of suprapubic drainage fistulæ (Fig. 8).

The use of the cystoscope to pass filiforms retrograde through a stricture in the urethra is troublesome, difficult and occasionally unsatisfactory. It is, therefore, desirable, when one has succeeded in passing filiforms to dilate strictures, to leave a thread in the urethra to avoid having to employ the cystoscope at the next seance. This thread must be drawn through the urethra by the filiform when it is removed. To accomplish this, we have had made a conical connecting piece through which the thread may be passed, knotted, attached to the filiform (Fig. 9, No. 1) and then drawn through the meatus and out the suprapubic fistula by the filiform (Fig. 9, No. 2). The urethral and vesical ends are then tied together so as to prevent escape (Fig. 9, No. 3). Braided silk threads are usually employed, but as these have a tendency to accumulate calcareous deposits, I have more recently used a silkworm gut, which has no such drawback. In order to attach the silkworm gut, it is simply introduced through the coupling piece, bent firmly together, pulled out until a small loop remains, a bit of

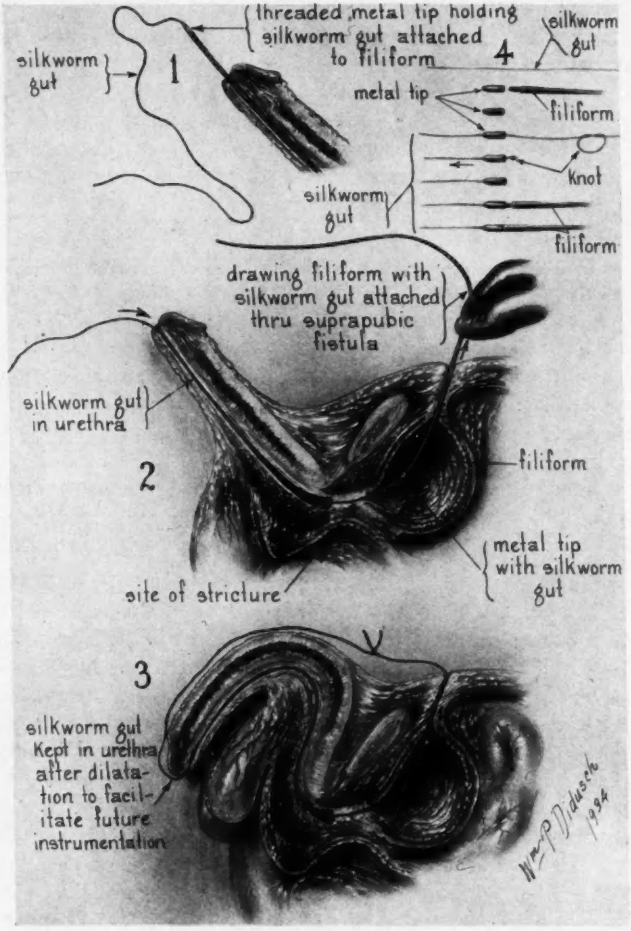


Fig. 9. No. 1. Attaching thread to filiform by conical coupler. No. 2. Drawing thread through urethra, bladder and suprapubic fistula. No. 3. Silk thread or silkworm gut left in place to facilitate passage of filiform next time. No. 4. Method of attaching silkworm gut to conical coupler and then coupler to filiform.

loose cotton placed in the loop to prevent its being drawn through when traction is made. By this homely method (Fig. 9, No. 4) silkworm gut can be used to draw filiforms through the strictured urethra for subsequent dilatations. A knot can also be used.

POSTOPERATIVE URETHRAL DILATATIONS

It is now my practice, after plastic operations in which dilatations must soon be carried out, to leave a fine thread of silkworm gut in

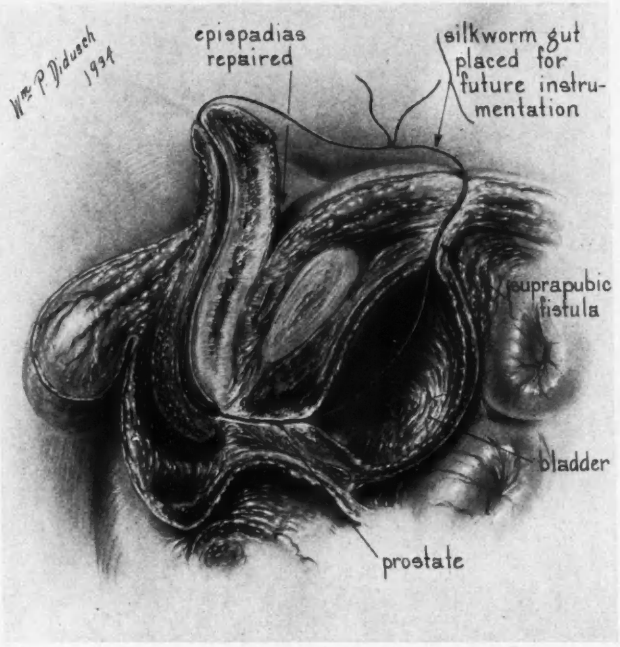


Fig. 10. Suture still in place after withdrawing suprapubic drainage tube in a case of Young's double sphincter and penile plastic operation for epispadias.

place. There it remains until some three to four weeks after the operation, when the first dilatations with filiforms and bougies are to be undertaken. Figure 10 shows a case of epispadias with incontinence, in which our double sphincter and penile plastic opera-

tion was carried out. The silkworm gut left in place emerges from the meatus and from the suprapubic wound. Some three to four weeks later it is employed to draw a filiform through, and this is followed by gradual dilatations with flexible bougies, and, in some

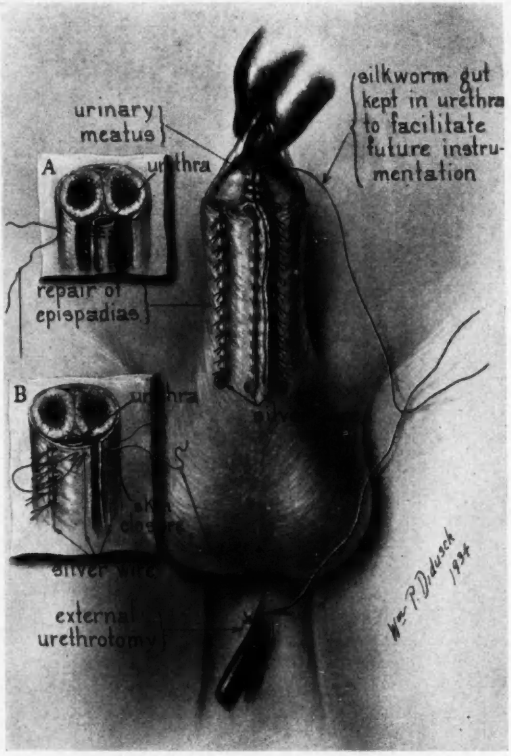


Fig. 11. Thread left in place after completion of hypospadias operation by latest technic with use of silver wires: *a*, formation of urethral tube; *b*, covering urethral tube with penile skin (overlapping method).

cases, metal dilators. The same method is employed in the double sphincter operation for incontinence after transurethral resections, or prostatectomy. In cases of hypospadias, the passage of filiforms and followers after the operation may often be the cause of serious

injury and breakdown of the sutured wound. By leaving a silkworm gut in the newly made urethra (Fig. 11) one end emerging from the perineal wound, and the other from the newly made meatus in the glans, several dilatations with filiforms and small followers can be ultimately carried out without danger or difficulty.

CONCLUSIONS

Not infrequently after various operations upon the urethra, necessitated by traumatisms, inflammatory strictures, incontinence or congenital defects (epispadias, hypospadias, et cetera) one must pass dilating instruments. The passage of filiforms through the dense stricture is often extremely difficult, particularly as they have a tendency to buckle upon themselves and prevent the passage of a dilator; in fact, the attempt to pass some such dilator may often lead to severe traumatism, the operator not realizing that the filiform has buckled and broken. New instruments and technical methods have been described to obviate these difficulties, first a series of urethral tubes which facilitate the discovery of the urethral lumen in the strictured area, and also prevent the buckling of the filiform when it and the attached, dilating follower are passed. The use of the catheterizing cystoscope to dilate a stricture of the deep urethra, by passing filiforms retrograde, has been described, and various technical devices for joining one filiform to another, or to attach a silk thread or silkworm gut, which is to be left in place to conduct other filiforms through the strictured region at subsequent seances, have been depicted. By means of these simple mechanical devices, the postoperative care of various urologic operations has been rendered much more accurate and satisfactory.

DISCUSSION

PROFESSOR CAPORALE (Torino, Italy): I am sorry for my little knowledge of English, and I ask your pardon.

I thank you, Mr. President, and all the members of this Congress, for the privilege of attending this meeting. I have for all the members the greetings of the President of the Italian Association of Urology and of the President of the Italian Association of Surgery, Professor Alessandri.

I am very glad to have heard the lecture by Dr. Livermore. I have studied this question, and have had the same experience as Dr. Livermore. Last year I was present at the meeting of the Italian Urological Association. I made a study of cases of hypertrophy of the prostate. I made many resections of the prostate. My conclusion is perhaps the same. It is necessary to select the cases, and if you select the cases you will have good results.

I used very successfully the instrument of Dr. McCarthy, and I know if you use the instrument with the same indication as set forth by Professor McCarthy, and if you use it in selected cases, you will get good results. The mortality will be low, the hospitalization of the patient will be little and you will have good results in all the cases.

DR. ARTHUR B. CECIL (Los Angeles, Calif.): One of the principal things, I think, our studies and discussions of resectoscopy has done has been to give us the mortality rate of suprapubic prostatectomy. I never before knew what this was and I am convinced that it will take the development of some other procedure before we will know the true mortality rate of resectoscopy. I am sure that as resectoscopy is at present performed the mortality rate cannot favorably compare with a similar group of patients operated upon by perineal prostatectomy. However, prostatic surgery should be removed from the field of emergency procedures and this is one of the principal things that resectoscopy has done and is going to do more and more. It is undoubtedly the method of choice in all 1 and 2 types of cases of prostatic obstruction. In the more advanced cases it is my opinion that perineal prostatectomy offers a lower mortality rate and a far higher cur-

ability rate. One of the urological services at the Los Angeles General Hospital has recently reported that patients on whom resectoscopy has been done are now returning for further treatment at the rate of one per week.

DR. J. F. MCCARTHY (New York City): I am wondering whether I understood Dr. Livermore to announce a mortality for suprapubic prostatectomy of 40 to 50 per cent. Am I right, Dr. Livermore?

DR. LIVERMORE: Right, yes, sir; in all hospitals throughout the country.

DR. MCCARTHY: I thought I misunderstood you.

The mortality rate given by Dr. Cecil here was 4 per cent. I believe there is a happy medium between these figures. We might say in all fairness a minimum 10 per cent. Thomson Walker, at the International Congress of Urology held in London last July, announced 18 per cent mortality in the general service hospitals, and about 10 per cent in special hospitals.

It is not my intention to discuss resection. It is sufficiently adolescent to protect itself. I merely wish to advise those of you who are doing resections and who have difficulty with hemorrhage, as we all do occasionally, please to remember that the compression bag used at the time of operation is a replacement for coagulation; also to remember that every time urethral tissue is electrically coagulated, especially in a diffuse bleeding urethra, when coagulation may be long drawn out, one must not forget that nature must laboriously resolve these coagulated areas, thus prolonging convalescence. The compression bag thus used is a replacement for coagulation and automatically implies shortened urethral repair, a most important factor.

Moreover, one should avoid too careful a resection in the region of the verumontanum because at that particular point one is liable to infect the seminal vesicle and the prostatic ducts. The whole subject is still an open one. Its stabilization must await reports of late microscopic and cultural characteristics of the prostatic secretion. Unless and until we have such findings, the whole question is still an open one.

PRESIDENT CAULK: Gentlemen, I asked Mr. Joly if he wouldn't

open the discussion. He said he had other papers that he would like to talk about, but I still would like to hear from him, and I know every one in the room would.

MR. J. SWIFT JOLY (London, England): Mr. Chairman, it is awfully kind of you indeed to ask me to speak. I am afraid I have got nothing to add about prostatic resection. We in our country do only tens of cases for the thousands you do here, and I am afraid we are still, most of us, much more inclined to do the open suprapubic prostatectomy. We may be wrong in that and we shall be exceedingly grateful if we can find out the true state of this very important question over here.

With regard to Dr. Clark's paper on replacement of the prostate by this huge calculus, these cases are extraordinarily interesting. There are a few cases where you can get a complete replacement of the gland without any appreciable communication between the cavity in which the calculi form and the urethra. I have had one case in which the gland was completely replaced, apparently, by calculi, somewhere between 600 and 700 stones in the prostate. I didn't count them; the sister did. It took me a half hour to scrape them out. But a most careful examination of the urethra, both before operation and during operation failed to show the slightest communication between the urinary passages and the prostate itself.

One gets cases, of course, where there are huge numbers of minute calculi in the prostate. But in these cases also one has failed to find any communication between the urethra and the cavity in which these stones lie, other, of course, than the ordinary prostatic ducts. So I believe in certain cases these great masses of stone can form in the prostate and from the prostatic secretion.

Mr. President, I thank you.

DR. BRANSFORD LEWIS (St. Louis, Mo.): I want to thank Dr. Livermore for his excellent report on this subject. I think it is more a report of experience in prostatic resection than it is an evaluation of the subject, because I do not think an evaluation is complete unless prostatectomy is included in the discussion.

I am glad to see the greater respect that is being according transurethral prostatic revision, including both resection and the punch operation, as manifested in the papers that have come out in the past year. This was also manifested in the symposium that was pre-

sented at the American Urological Association last year, when the whole morning was spent on this subject and never once was resection called a minor operation; not a word was said about the absence of mortality, of morbidity and of adverse results that often came along with the favorable ones. In other words, due respect is now being accorded to transurethral revision that was lacking two or three years ago when the urological profession seemed to go wild in advocating these procedures and didn't stop to give attention to the drawbacks.

I do not participate in the belief that prostatic resection is always the safer of the two procedures. In certain cases prostatectomy offers greater protection than does any form of instrumental revision. So if that view is correct there must be retained a position for prostatectomy that was not accorded to it two or three years ago. I remember when the expression, "Prostatectomy is obsolescent or already obsolete," was widely prevalent.

Lately I have heard some of my urological friends who were most enthusiastic for prostatic resection say that they reserve 15 or 20 per cent for prostatectomy. I wish to congratulate them on their "second thought" on this subject. I myself have a tremendous regard for that wonderful procedure of prostatectomy; I want to see our friends retain it in a position of usefulness and retain their ability to do prostatectomy when it is needed, and it is needed in many cases. Please don't get the idea I am making war on prostatic resection; I am not decrying it and never have said anything against it, even in the "Moonlight and Roses" paper. Dr. Carroll and I said definitely in that paper that we were criticizing the misrepresentation of the safety and innocuousness of this procedure. We did not criticise the instrumental equipment, the operations or the methods, but we took exception to the sanguine statements that were wildly rampant at that time.

Dr. Frank Hinman (San Francisco, Calif.): I am interested in this work of Dr. Lower and his associates. It would seem that urologists will have to become endocrinologists to a certain extent. There is a very close homology between the sexual organs of the male and the female. The female is the result of active growth of the Müllerian ducts with degeneration of the primary excretory ducts and the male is the opposite, the result of an active growth of the primary excretory ducts with degeneration of the Müllerian

ducts. The ultimate sexual organs are homologous in a great many ways.

This is true also of hormones excreted in the urine. Women during pregnancy excrete a hormone which gives, when injected into infantile female mice and rats, certain very definite reactions. These reactions have been characterized by Zondek as reactions 1, 2 and 3, according to whether there is ripening of the graafian follicle, formation of hemorrhagic cysts or luteinization. An additional reaction not described heretofore is definite hypertrophy of the uterine horns. This reaction occurs in rats typically and is given by some hormones and not by others. There is a difference in the reaction of stimulation according to the origin of the hormone and according to the animal which is used for the test. The mice, the rats and the rabbits which have been used give some difference in reaction according to whether the hormone comes from the pituitary body, whether the hormone is from a pregnant woman or whether the hormone is generated in an embryonal growth such as tumor of the testis. These three conditions are known to give gonadotropic types of hormones, and this stimulation of growth of gonads and genitals occurs when the urine is injected into infantile female animals.

What reactions will follow the injection of these hormones into infantile male animals has not been determined. I think this will prove interesting. Connor in California has been injecting urine of pregnant women which contains a genitotropic, so-called gonadotropic hormone, into dogs, and he finds that a very definite hypertrophy of the prostate occurs as a result. If he castrates these dogs and injects urine containing the hormone, hypertrophy of the prostate does not occur. This experiment would seem to demonstrate that the hormone acts through the testicle.

There are several preparations on the market for clinical use. The clinical application of gonadotropic drugs raises this question. Clinical use of the gonadotropic hormone obtained from the urine of a pregnant woman might produce hypertrophy of the prostate along with stimulation of the sexual functions of that individual. On the other hand, if we find a hormone which does not produce hypertrophy of the prostate but does stimulate the gonadal functions, we will have our ideal clinical drug. Hypophysin, which is put out by Winthrop Chemical Company, has been used effectively

in two or three cases of impotence. These people, however, are young people and whether one would dare to continue the use of these injections without fear of producing prostatic hypertrophy remains for future experimental demonstration. Another drug on the market, antipituitrin, is not nearly as potent as hypophysin.

The interesting thing is the close homology between the hormones of the male and female. This relationship will have to be established by further and future experimental work. Work so far has been largely concerned with reactions in females. What is wanted is an understanding of the gonadotropic and stimulating properties of these hormones on male animals.

DR. HUGH H. YOUNG (Baltimore, Md.): I am much interested in Dr. Livermore's evaluation of prostatic resection, in which he shows excellent results with this method, but admits that there are many cases in which prostatectomy may still have a place.

Reports from various parts of the country indicate that the attitude of the urological profession generally is not nearly so enthusiastic about the use of resection in all types of prostatic obstruction as it was a year or two ago. It seems that we are going through something of the same history that we did with the Bottini operation years ago. Older members here will remember quite well how the Bottini operation almost completely swept prostatectomy off the boards for a few years. The simplicity of the operation, the fact that an electrically heated platinum blade could be drawn through the prostatic lobes, and destroy enough tissue in two to three minutes to do away with the obstruction, seemed so simple that it was widely adopted. It was only after many serious complications had occurred (extensive suppurations, gangrene, septicemia, extravasation, recto-urethral fistulæ, secondary hemorrhages, etc.) that this apparently slight operation proved to be dangerous. I, too, was swept off my feet, employed the operation in some seventy-five cases with an ultimate mortality of 7.5 per cent, and some of the complications above described. I then realized that the operation was not ideal, went back to prostatectomy, devised my tractor, developed the perineal technic, with a gradually lessening mortality rate, until for three and one-half years there was no death in 198 consecutive cases.

After this I employed only perineal prostatectomy until I encountered certain types of contracture at the vesical orifice (bars,

valves, etc.) in which I found that with a prostatic excisor I was able to attack these cases satisfactorily with a far shorter convalescence, and equally good results. When I attempted to use my punch operation in cases of pronounced hypertrophy, the results of the transurethral surgery were like the Bottini operation—unsatisfactory.

The main trouble with the punch operation was difficulty in completely stopping the bleeding. By means of a cautery blade, which

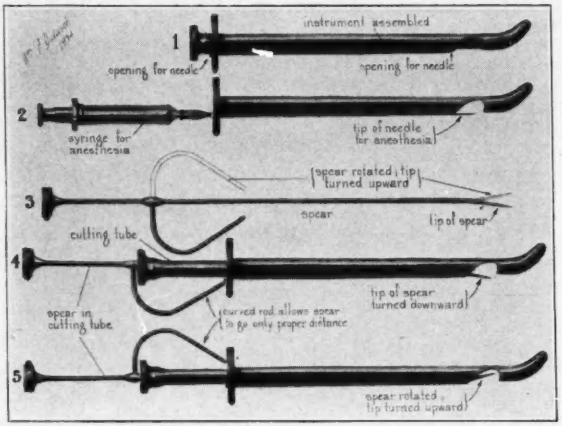


Fig. 1. (1) Young's punch with a tube attached through which a long needle can be passed and anesthesia injected into the tissue. (2) A syringe attached to a long needle and the tip of the needle emerging near the fenestra. (3) A spear with the tip at an angle to the shaft. It is inserted into the inner cutting tube and plunged into the tissue. As the spear is rotated, the tissues to be excised are drawn into the fenestra and held in position. (4) Spear placed in punch, with tip turned downward. (5) The spear has been rotated, showing the tip turned upward.

I brought out in 1911, hemorrhage was arrested, but necrotic tissue formed occasionally a postoperative complication. I believe that Caulk, in his simplification of the cautery punch, has made a very valuable addition, but I still employ my punch operation, with the addition of a spear (Fig. 1), by means of which more tissue may be drawn into the urethra, and larger pieces excised. The hemorrhage can usually be promptly arrested by cystoscopic fulguration,

but in one case recently an artery evaded us, and for the first time in more than 600 cases, in which the punch had been employed, I found it necessary to do suprapubic drainage to pick up the artery and stop the hemorrhage.

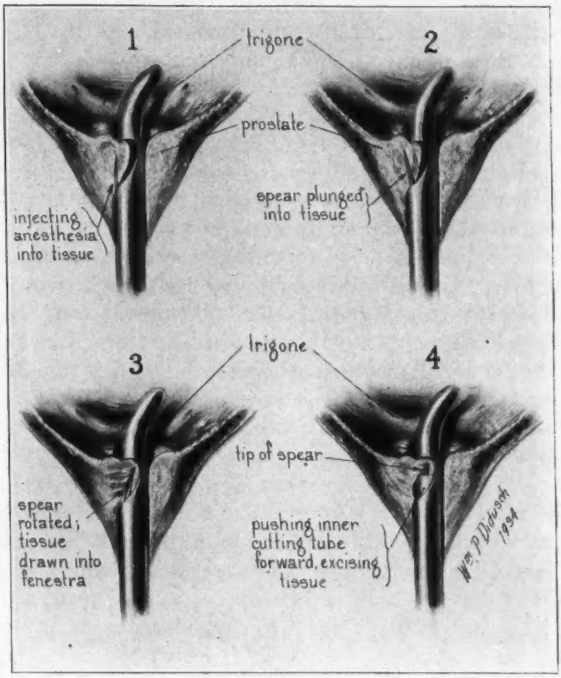


Fig. 2. (1) Punch turned to right with tissue partly engaged in fenestra. The needle has entered the tissue and anesthetic is being injected. (2) The spear, turned outward, has been plunged into the tissue. (3) The spear rotated, drawing a greater amount of tissue into the fenestra. (4) The inner cutting tube is excising the tissue as the end of the spear holds it firmly in position.

By adding a delicate tube on the outside of the sheath, in which a fine needle is carried to make injections of novocain into the various portions of the prostatic neck (Fig. 2), the operation can now be done with little pain.

I am still of the impression that although much tissue can be

removed, it is better to employ perineal prostatectomy for the pronounced hypertrophies, in which a clean enucleation of the entire hypertrophied tissue may be carried out with less danger than is shown by the transurethral statistics of Caulk.

At the Brady Urological Institute transurethral operations with my punch, with Caulk's cautery punch, and with various types of electrical resectors have been employed during the past two years so as to obtain comparative statistics. The number of cases is as yet too small to make any positive assertions, but I have become more and more convinced that transurethral surgery should not replace perineal prostatectomy in cases of pronounced hypertrophy of the prostate. While it is quite possible, even in large cases, by prolonged effort, to ream out a good portion of the lobes, perineal enucleation is quicker, more complete, leaves a clean wound, gives the operator a chance to thoroughly stop all hemorrhage, provides excellent drainage, and gives better and more lasting results than the transurethral method. Transurethral surgery is certainly here to stay, but the instruments that are to be used in the future are, perhaps, not yet perfected. It is important not to overdo. One must realize that he is dealing with very powerful agents, and that it is possible to do great harm.

Last year there came to me a patient in whom the external sphincter was so badly injured in a transurethral resection that incontinence occurred, although the resectoscopist had left behind a very large left lateral lobe. The verumontanum was also destroyed.

With care, and by confining the operation to much smaller cases, better results and a lower mortality will be obtained. One very definite result has been the abandonment of suprapubic prostatectomy, particularly the two-stage operation. The fearfully high mortality acknowledged by Keyes and others is, I believe, largely responsible for the great vogue of transurethral operations. Preliminary drainage of the bladder can be very satisfactorily carried out with the simple inlying urethral catheter. If suppurative urethritis, pain, et cetera, render this unsatisfactory, a quick perineal incision through the bulbous urethra, with insertion of a mushroom drain, will give satisfactory results with far less danger. With perineal prostatectomy employed for the important hypertrophies, and the transurethral methods reserved for much less extensive

cases, I believe we shall have in the future a systematic method of attacking prostatic obstructions with far less mortality than has been general in the past.

DR. HERMON C. BUMPUS, JR. (Rochester, Minn.): I wish to discuss that phase of Dr. Livermore's paper relative to the incidence of febrile reactions following resections, and his emphasis on the intravenous use of methenamine. Some years ago, when such febrile reactions were common, we adopted the routine administration of methenamine intravenously.

I have always disliked the giving of drugs as a routine procedure instead of as symptoms indicated. In addition, the dosing of the patient with methenamine tends to give a false sense of security against infection.

What caused the reactions rather than how to cure them seemed the important point and by a careful study of the bacterial flora of the urine at admission prior to operation, immediately after operation, and during convalescence, we discovered that febrile reactions do not occur unless some new organism is introduced into the urinary tract. When the cultures showed the same flora before as after operation, severe febrile reactions did not occur.

The task then was to find at what point these new organisms were introduced. We discovered that we had been lax in our method of catheter drainage the first forty-eight hours after resection, permitting the catheter to drain directly into a urinal. Urinals quickly become contaminated and catheters tend to slip out and come in contact with the bed linen, in which case at the next irrigation the bacteria from the linen, frequently of rectal origin, are washed up into the bladder.

Under our present technic the catheter is wrapped in a sterile towel at the time of its insertion. When the patient is back in bed the catheter is attached to a 3 foot sterile tube leading to a sterile bottle. This system is never allowed to be opened except under the most rigid aseptic precautions, and when the bottle is full it is not emptied for then the tubing may come in contact with an unclean surface such as the mattress, sheet, or floor; instead the nurse replaces the full bottle with an empty sterile one.

Since adopting these precautions and adhering to the most rigid aseptic technic before, during and after resection, our incidence

of febrile reactions has been much reduced, so that of the 721 patients resected during 1932-1933 the postoperative temperature remained below 101° in 79 per cent of the cases.

Doctor Cecil mentioned the large number of recurrent cases seen at the Los Angeles General Hospital. During 1933 there were 451 resections done at the Mayo Clinic with five deaths. Of this number twenty-five, or 5.5 per cent had had previous resections, nineteen at The Clinic and six elsewhere. Included in the 451 resections were ten patients who had had a previous prostatectomy. Methods of treatment, like individuals, are seldom perfect.

DR. A. J. CROWELL (Charlotte, N. C.): I promised myself before I left home I would keep my mouth shut at this meeting, but I must enter a word of warning against undertaking to resect the large adenomatous glands until you have done a great many of these operations. You will have uncontrollable hemorrhage if you are not careful. We did our six hundred and seventy-fifth resection last Wednesday. We are thankful that we haven't had to open the bladder a single time to control hemorrhage. We have had to fulgurate one patient a second time and one a third time to control hemorrhage. Only last Saturday we had to do a fulguration on a patient upon whom we operated Wednesday, to control severe secondary hemorrhage. Within twenty-four hours after operation he had a hard chill and his temperature went to 108, the highest I have ever seen in an adult. By using ice packs and alcohol sponges his temperature came down within a couple of hours to 101 and so remained for about twenty-four hours, since which time it has been practically normal. We had to fulgurate the third day after operation to control a severe secondary hemorrhage. There was no reaction following this operation and the patient has had no further complications.

We are beginning to feel more and more that there are certain very large adenomatous glands that should be removed, either suprapubically or perineally.

Again I want to enter a word of warning about incontinence. In operating you must stay posterior to the verumontanum or you will injure the external sphincter and have incontinence; not only that but likely the patient will have epididymitis as a complication. If you get too close to the verumontnum, you will likely get into the ejaculatory ducts and thus encourage epididymitis.

I think it rather dangerous to use spinal anesthesia in resections. The gas formed in the bladder in doing a resection will cause a rupture of the bladder if you are not very cautious. If you do a sacral and transcaudal operation, the patient will let you know when the bladder is full of water or gas but if the operation is done under spinal anesthesia, all sensation is gone and you will have no warning until the bladder is ruptured. This has occurred in some cases of which I have knowledge.

Now as to fatalities. We have had two in our series that we charged up against the operation. One of them was a man who died about two weeks ago, eighty-two years of age. He had had a suprapubic drainage for seven months and came into the clinic suffering profound shock from hemorrhage. We kept him for about a month and sent him home to build up. He returned and was resected. About ten days after operation he began having secondary hemorrhage and continued, one after another, in spite of transfusions and other remedial agents. He finally died of pneumonia six weeks after the operation.

DR. JOHN H. CUNNINGHAM (Boston, Mass.): I am not going to talk at length about resection. I am only going to bring to your attention a matter that rather suggests that incontinence does sometimes occur after this procedure in which we are all so interested. A well known company selling urologic instruments has been carrying a device called the incontinence clamp, which I invented years ago for a patient upon whom I did a radical removal of a carcinomatous prostate by the Young method. The agent selling this clamp recently told me, with the popularization of this new electric procedure, that the sales of these clamps had mounted very rapidly. He said also that the increase in sales of the clamp was coincident with the failure to sell suprapubic tubes as before. In other words, the suprapubic tube failed to sell and the incontinence clamp took its place.

I asked him how many of these clamps he sold last year. He said, "Strange as it may seem, one a day. We sold 365 of these incontinence clamps during 1933 and the sales are picking up."

I asked, "How many did you sell two or three years ago?"

"Well," he said, "if we sold twenty, we were doing well."

This is simply information that comes from a man who sees and sells to the urologists all over the country and gives a suggestion

that perhaps incontinence is occurring in consequence of this procedure. I am not here to recommend the clamp and hope that you gentlemen who are employing electrical resection will not need to use it.

DR. GEORGE R. LIVERMORE (Memphis, Tenn.): I have nothing more to add except to state that prostatectomy, too, has its bad results. I have seen cases where incontinence occurred. I have also heard of cases where the peritoneal cavity had been entered and the rectum lacerated, and many cases of recurrence after prostatectomy have been reported. I have also done a punch operation for contracture of the bladder neck following prostatectomy, and I have heard of some mortality. I do not say that all cases are suitable for resection. I am still doing prostatectomy, having done six in the past two years. I do not say that every one should do resections. I am giving you the evaluation of my results in 100 cases. I do not think they are perfect and therefore want to improve them. I want to help myself and I want to help you.

DR. WILLIAM E. LOWER (Cleveland, Ohio): I was very appreciative of Dr. Hinman's interest in the endocrines. I am sure, with his exacting way of investigation that the relationship of the endocrines to the problems of the genito-urinary surgeons, will be greatly advanced. It was recently reported that in a group of eleven castrated women there was found a substance in the urine of two which, when injected into male animals, produced very definite atrophy of the prostate. We may be on the eve of finding something worthwhile. I am not a prophet, but I hope that, before many years have passed, this controversy of the mortality of the different methods of prostatectomies will cease, because we shall have no prostatectomies to do.

DRAINAGE PROBLEMS IN UROLOGY

N. P. RATHBUN, M.D.
Brooklyn, New York

The matter of adequate drainage is of vital importance in all branches of surgery; it is of particular importance in urology, since we have always to deal not only with wounds which are usually infected or potentially infected, but also with the presence of urine, also usually infected, passing through a series of relatively narrow channels.

It would, of course, be folly in a short paper to undertake a discussion of all phases of these problems that arise in the practice of urology. Such an attempt might easily evolve into a textbook on urology. It is the purpose of this paper to discuss only a few of these problems, including a few in which the technic is fairly well standardized, a few others about which there may be some differences of opinion and, finally, to present for consideration a type of drainage material which, while neither new nor original, may be new to some and which has certain advantages which would seem, in my opinion, to warrant a wider usage.

I remember in my very early days being profoundly impressed by a paper of the late Charles McBurney, at that time professor of surgery at the College of Physicians and Surgeons. It was one of the very few contributions which he made to the literature and was, I think, his last contribution. It was a very short paper but, like all of his papers, contained a declaration of a fundamental principle. He maintained that every wound, intentional or otherwise, made into or through the skin was potentially infected; that while we could beyond any peradventure of doubt sterilize our instruments, that we could reasonably expect to remove all bacteria on the surface of the skin, we never could be sure of destroying all bacteria that were *in* the skin. He further maintained that nature, unless unnecessarily handicapped, was well able to take care of this factor by means of her own inherent defense mechanism, phagocytosis, et cetera. He further stated that following every wound there was a certain amount of lymphatic and serous exudate which did no harm provided it had a free vent; lacking this it

might and often did induce a pressure necrosis, perhaps microscopic in degree, which provided a suitable culture medium for bacteria, and this might turn the scale against nature's defenses. On the basis of that reasoning he proposed drainage in practically all wounds. I believe that was sound reasoning thirty years ago and I believe it is sound reasoning today. I have been influenced throughout my entire professional life by the principles enunciated in that paper. I do not practice nor advocate the use of drains in all wounds, but I do make it a point to suture skin wounds loosely, leaving ample room between stitches to take care of any drainage that might occur. I do not believe that overzealous attempts at accurate skin approximation, including subcuticular, continuous or closely placed interrupted sutures is good surgery. This applies even to plastic surgery. I can understand how one might in certain nephrectomies close the entire wound with no form of drainage. Most of us, I think, use a small drain at the dependent angle of the wound with an added sense of security and no material delay in convalescence or wound closure.

All wounds made in the kidney or kidney pelvis require not only drainage of the surrounding tissues, but also drainage of the organ or cavity invaded. Wounds of the kidney pelvis are adequately drained in the majority of cases by the simple expedient of loose suturing or no sutures at all. In cases of gross infection or in pyelotomy for multiple soft calculi, I believe it is well to supplement this with a soft rubber tube anchored in the pelvis. All wounds in the kidney parenchyma, for whatever purpose, should be supplemented by drainage of the kidney pelvis through a soft rubber tube brought out through the kidney wound. This should be done not only for the ordinary purposes of drainage, but also as a means of lessening the likelihood of secondary hemorrhage. The neglect of this little point has, I am sure, resulted in the sacrifice of a great many kidneys. I plead guilty to a few in my own practice. In plastic operations on the kidney pelvis I believe it is accepted practice to supplement the drainage provided for by sutures not too closely placed with an added rubber tube drain brought out through a stab wound in the cortex.

Open wounds of the ureter, of course, require drainage. This applies with particular force to wounds made deep in the bony pelvis. Here the type of drain and the period of time over which

drainage is maintained are of vital importance and will be discussed later in this paper.

While the urologist has relatively infrequent occasions to invade the peritoneal cavity, he is however called upon occasionally to do this in such operations as abdominal nephrectomy, ureter transplants, certain types of bladder resections, et cetera, and he should be prepared to deal with the special problems involved: protection of the peritoneal cavity and prevention of adhesions to surrounding organs. The quarantine or coffer dam principle as elaborated by Coffey in his operation for uretero-sigmoid anastomosis would appear to cover this situation admirably and is undoubtedly familiar to all.

DRAINAGE OF THE CLOSED URETER

While I have no desire to resurrect the somewhat controversial issue of ureter stricture at this meeting, nor do I wish to provoke any such discussion (some of it bordering on acrimony) which was indulged in several years ago, I do, however, wish very briefly to express one thought: I believe that Hunner, when he focused our attention on the ureter several years ago, made a very valuable contribution to urology. While I am quite willing to admit that, in my opinion, stricture of the ureter as a pathologic entity does not occur with anything like the frequency that Hunner would have us believe, neither do I go all the way with Hunner in ascribing such a wide variety of remote results to this lesion. I do, however, firmly believe that obstructive lesions, including stricture, in and about the ureter, particularly in its lower third, are of common occurrence. Many of these cases present a train of symptoms which are readily amenable to the simple expedient of ureter dilatation. I would suggest that in certain cases of hydronephrosis the patient be given the benefit of adequate ureter drainage before proceeding to radical surgery. I am well aware that in many cases the obstruction can be readily demonstrated at the uretero-pelvic juncture. These are not included in the group that I would treat conservatively. There is another group of patients, who complain of obscure kidney and ureter pain, in whom no definite objective pathology can be clearly demonstrated. These patients are not infrequently subjected to decapsulation, denervation and various other operative procedures. I would suggest that these

patients be given the benefit of a few dilatations. It will do no harm and may do some good. After all, patients are far more interested in the relief of symptoms than they are in a more or less academic diagnosis.

While there are many factors involved in the problems of urinary lithiasis, we are entirely sure of the importance of one factor and that is adequate drainage. I believe that all patients with renal or ureteral calculi, which have been delivered either through the natural channels or at operation, should have as a part of their routine after-care an occasional ureter dilatation.

DRAINAGE PROBLEM IN PROSTATISM AND PROSTATECTOMY

It is not within the scope of this paper to enter into any discussion of the relative merits of transurethral operations and operations done through open wounds. While admitting that transurethral procedures are destined to occupy an important place in prostatic surgery, I am convinced that formal prostatectomy will continue for many years to engage the time and attention of most urologists and the following remarks are based on that conviction.

I think it is fair to say that the matter of adequate drainage before and after operation has been of vital importance in the evolution of prostatic surgery and the reduction of its mortality and morbidity. I shall discuss only a few of the many problems involved.

Preliminary Catheter Drainage.—I am thoroughly addicted to this method in practically all cases. I think we will all agree that it is clearly indicated in cases where there is a large amount of infected residual urine. I think it is equally valuable in the opposite type of case with a relatively small amount of clear sterile residual urine and for a very different reason. I believe, as Cabot suggested many years ago, that it is good practice to expose these patients deliberately to a mild degree of infection and give nature a chance to establish a defense mechanism before more radical steps are taken. I realize that in taking this stand I may be out of step with what might be called the best thought of the day. I believe the present trend is toward the ideal of an entirely aseptic procedure. In my opinion this is a complete and total impossibility. I believe that, without exception, every patient who is submitted to any form of prostatic surgery passes through a period of infec-

tion. There are bound to be slips in the technic, to say nothing of the fact that even in cases with clear sterile urine the gland itself is infected in practically all cases. If the patient must have a period of infection let us have it at a time when he is best able to tolerate it.

It is a well recognized fact that the immediate convalescence following a perineal prostatectomy is apt to be smoother than that following the suprapubic operation. This is undoubtedly due in large measure to better drainage. Following suprapubic enucleation a cavity is always left which at best it poorly drained and is a potential source of trouble. This can be corrected in a measure, if one has the adequate exposure of a one-stage operation, by carefully trimming away the overhanging ledge on the proximal side of the cavity. I do not think it is desirable to close or cover this cavity by means of suturing as has been suggested by several surgeons. Neither of these procedures is feasible in the two-step operation. Here, I think, we should keep constantly in mind the fact that we have such a cavity and provide for it by adequate and sufficiently prolonged suprapubic drainage. We should not be too eager about early strapping and early closure of the suprapubic wound. Like most urologists, I have gone through various cycles in connection with many of the details of prostatic surgery, particularly in reference to the management of bleeding. For several years I was addicted to the use of a gauze pack which was sometimes left *in situ* for several days. After a while it dawned upon me that I was having a rather high incidence of toxic psychoses. I believe this may have been due in part to poor drainage of the prostatic bed. I am now using the Hagner or Pilcher bag and having less trouble with psychoses. This is perhaps one argument against the use of the gauze pack.

Suprapubic Drainage.—In doing a suprapubic cystotomy I believe we should make an effort to preserve the vesico-pubic fascia as was stressed by Morton before this society a few years ago. If the space of Retzius is entered it should be adequately drained and drainage mantained until granulations are established. Many years ago I had a death from prevesical infection in a case which was left in charge of a young assistant. The drain was removed at the first dressing and was not replaced.

Seminal Vesicles.—I am quite sure that infection of the seminal vesicles as a complication of prostatic surgery occurs more commonly than is generally supposed. Attention was called to this fact several years ago by Boyd and a year later by the present writer. I feel that neither of those papers attracted the attention to which they were entitled. Certain it is that one sees very little about the subject in the literature. I have seen a number of patients who, following prostatectomy, continue to have marked frequency and dysuria even though the obstruction is entirely relieved. In many of these cases one can readily determine the presence of a vesiculitis by rectal palpation and most of these patients are promptly relieved by simple massage. I have long had a feeling that some of the cases of more or less intractable toxic psychoses in which drainage of all other probable sources of infection would appear adequate, might be explained on the basis of an infection in the seminal vesicles. I have even contemplated surgical drainage in some of these cases, but never have been able to justify myself in doing it. Drainage could, of course, be established by way of the perineum or, as has been recently suggested, directly through the bladder wall. All this, of course, without clinical data is more or less idle speculation but it is presented simply as a thought for consideration.

DRAINAGE MATERIAL

I should like to discuss briefly the matter of drainage material. The materials ordinarily employed are some form of tubing, usually rubber, occasionally glass, rubber tissue, and various forms of gauze or some combination of two or more of these agents. Obviously, since these materials are so commonly used they must be adequate and reasonably satisfactory. However, I venture to suggest another type of drain which I am sure possesses certain very definite advantages over any of the other drains in common use. The material which I suggest is ordinary raffia or African grass, commonly used by florists and easily obtainable from them. I have used it in my practice for fifteen years with entire satisfaction and I feel that I am in a position to vouch for one essential requirement. It does drain, by capillary attraction, of course. While it provides an ideal drain for any wound, I think I can best illustrate its advantages in connection with drainage deep in the pelvis

following operations on the lower ureter, bladder resections, et cetera. Adequate drainage in these cases is of vital importance. It is vitally important too that there should be no danger of trauma to surrounding structures. I have heard of instances where rubber tubes have eroded one of the iliac veins with resulting serious or fatal hemorrhage. Raffia has the further advantage in that it is a simple matter to reduce the amount of drainage gradually and at the same time feel sure that adequate drainage to the entire depth of the wound is maintained as long as may be required. One or more strands may be loosened or entirely removed with each daily dressing until only one or two remain. These may be left until we are absolutely sure that no further drainage is required and then perhaps a day or two longer. These last strands are finally removed, leaving a tiny sinus tract which promptly closes.

The method of preparation is briefly as follows: the raffia is obtained from the florist in loose bundles, placed in a pillow case and boiled for three minutes; the wider strands are now selected, pressed flat and cut in 14 inch length. They are now placed in packages containing twenty strands in each and tied together near one end with catgut. These packages are wrapped in gauze and autoclaved for forty-five minutes at 18 to 20 pounds pressure on three successive days. Immediately before using they are immersed in boiling water for one moment. This is for the purpose of making the raffia more pliable.

In conclusion, I should like to make acknowledgment to Dr. John E. Jennings, who first introduced this method in the general surgical service of the Brooklyn Hospital, where it has been in constant use ever since.

TREATMENT OF TUBERCULOSIS OF THE URINARY BLADDER

GILBERT J. THOMAS, M.D., and (by invitation) THOMAS J. KINSELLA, M.D., and CHARLOTTE C. VAN WINKLE, M.D.

Minneapolis, Minnesota

Tuberculosis of the urinary bladder is pathologically a secondary lesion in the urinary tract. From the patient's standpoint it is of primary importance as it produces the disturbing symptoms from which he seeks relief. Coming as a relatively late complication of genito-urinary tuberculosis, cystitis is too frequently present for a long time before its true significance is recognized. The symptoms may not disappear promptly after the surgical removal of the renal focus or after other therapy is instituted, but may continue to torment the patient for a considerable period of time. In the various papers that we have presented during the last several years we have not only made the statement that tuberculosis of the bladder is a secondary lesion, but we have insisted that if the patient is examined early enough the urologist should be able to make a diagnosis of the primary urinary infection in the kidney before bladder involvement occurs.

The lesions produced by tuberculosis in the bladder when observed through a cystoscope may vary from a limited inflammatory areola adjacent to one ureter to a most extensive angry sloughing ulcerative cystitis in the advanced stages. If early, the lesion is a localized area of inflammation, or an ulceration in the base of the bladder, usually more marked on the side of the involved kidney. The lesions may be located entirely in the region about the corresponding ureter. These may extend so that extensive areas including the dome of the bladder are involved. There is apparently no consistent correlation between the extent of disease in the kidney, the amount of ulceration in the bladder and the degree of symptoms as presented by the patient.

MODE OF INFECTION

We believe that infection of the bladder occurs following the continuous irritation of the mucosa from urine infected with

tubercle bacilli. As the mucosa has its resistance lowered a receptive soil is produced so that plantings of tubercle bacilli occur easily. If infected urine comes into the bladder continuously, new inflammatory areas develop. It is possible for inflammation of the mucosa of the bladder to occur at the meatus of the ureter secondary to a ureteritis. Since inflammatory areas may occur at some distance from an infected ureteral meatus, involvement of the bladder mucosa by continuity from this source only is not probable. We have observed areas of cystitis in the base of the bladder which we believe were secondary to tuberculous urethritis and prostatitis associated with a very minimal renal lesion. This infection apparently spreads along the mucosa directly from the prostate or urethra. Is a hematogenous route of infection of the bladder possible? Since the arteries located here are end vessels, a peculiar type of inflammation in this organ is observed following the deposit of infected emboli in these end vessels. Pan-mural cystitis is possibly an example of this type of chronic inflammation. Does a similar bladder condition occur during a tuberculous infection? Although engorgement of the vessels makes one wonder concerning the possibility of a hematogenous origin of this infection, a study of a large number of gross specimens, and microscopic sections, seems to indicate that the infection in the bladder probably comes from the planting of the bacilli directly on the mucosa. We have observed patients who have had a known tuberculosis of the kidney for many months, sometimes years, and whose urine has continuously revealed tubercle bacilli, both on smear and by guinea pig inoculation, and still the bladder may not become infected. When this situation is compared with the severe infection that is frequently encountered in the bladder associated with only a minimal renal lesion, one wonders what other factors must be present before cystitis develops. Our study does not clearly reveal the accessory factors which may be operative when the planting of the tubercle bacilli occurs so that ulcers eventually develop. We do know from clinical experiences that severe tuberculosis of the bladder with ulcerations usually occurs in a patient who has advanced lesions of tuberculosis and who has little or no resistance to the infection in any tissue. We also find severe cystitis in individuals who have long standing, bilateral renal infections. We have no evidence that trauma is a factor that may predispose the bladder mucosa to

tuberculous infection, although it is frequently found with other infections in the bladder, particularly when obstruction occurs at the bladder neck and over-distention results.

PATHOLOGY

From the postmortem material of Glen Lake Sanatorium we have selected for demonstration a few cases of proved tuberculous ulcers of the bladder. These show either tubercle bacilli at the

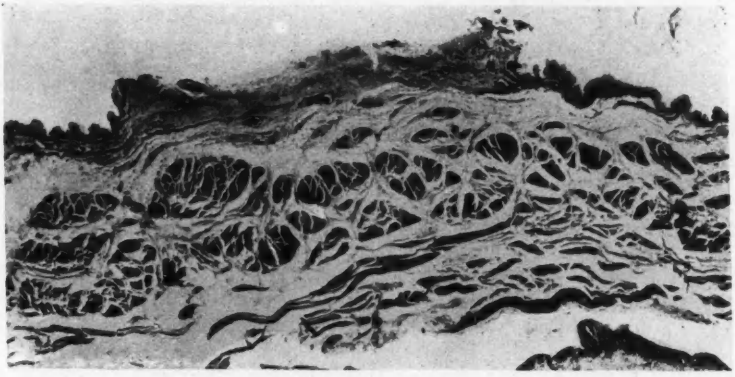


Fig. 1. Early stage.

base of the ulcers or tubercle formation in the surrounding tissue. An occasional specimen shows both tubercle formation and tubercle bacilli. We have found a number of early lesions corresponding to the spotty inflammation and congestion of the bladder without ulceration that is frequently observed through the cystoscope. No bacilli or tubercles have as yet been found in these inflammatory areas so their exact etiology is doubtful. We believe that they constitute early stages of inflammation preceding ulceration. Similar stages of inflammation can be traced in the evolution of ulcers in the intestinal tract.

Pathologically a number of stages of development of tuberculous ulcers of the bladder may be traced. They run a slow chronic course and show considerable fibrosis even when progressing. The small ulcers have a bright red raised edge and a greenish base. Figure 1 shows an example of this stage. The exudate at the base and

periphery contains many scattered tubercle bacilli. We have not found tubercle formation at this stage. There is usually considerable fibrosis and may be some muscle atrophy. The capillaries are congested and filled with necrotic material.

The gross appearance and microscopic section of a slightly later stage are shown in Figures 2 and 3. In this specimen the edges

Fig. 2. Gross lesions.

of the ulcer are thickened and fibrous. The base is necrotic and invades the muscle layer. In Figure 4 there is shown still greater fibrosis of the submucosa with atrophy and fibrosis of the adjacent muscle layer. The contraction of the fibrous scar tissue probably helps to keep the inflammation alive both by increasing the depth of the ulcerated surfaces which makes epithelial healing difficult and decreasing the capacity of the bladder. Tubercles are sometimes found in these later stages. In some they do not appear to

be part of a progressive lesion but rather one that is stationary or slowly healing. In other cases tubercles appear in a rapidly progressive tuberculous infiltration of the entire wall. Figure 5 illustrates this latter progressive type with tubercles and necrosis of the entire bladder wall.

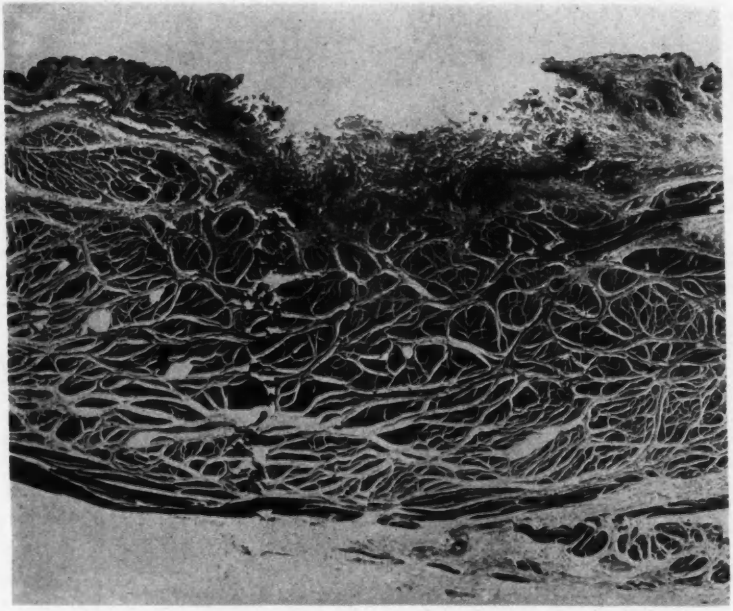


Fig. 3. Deeper ulcer involves muscle tissue.

TREATMENT

The ideal method of treatment of patients with genito-urinary tuberculosis would be to discover and adequately treat the renal lesions before bladder involvement occurs. This is apparently not feasible at present because of our inadequate knowledge, and probably never will be entirely accomplished because of the frequent absence of symptoms in the earlier stages of renal infection. If we fail in this preventive effort we should next direct our attention toward helping the patient build up resistance against tuber-

culosis, both generally and locally. In our experience bladder symptoms associated with vesicle tuberculosis have at times disappeared to a remarkable degree when the patient has had bed rest. Physicians generally, and urologists particularly, should take advantage of this method of treatment much more often than is being done at the present time. Years of experience have taught us that removal of the tuberculous focus in the kidney has a beneficial

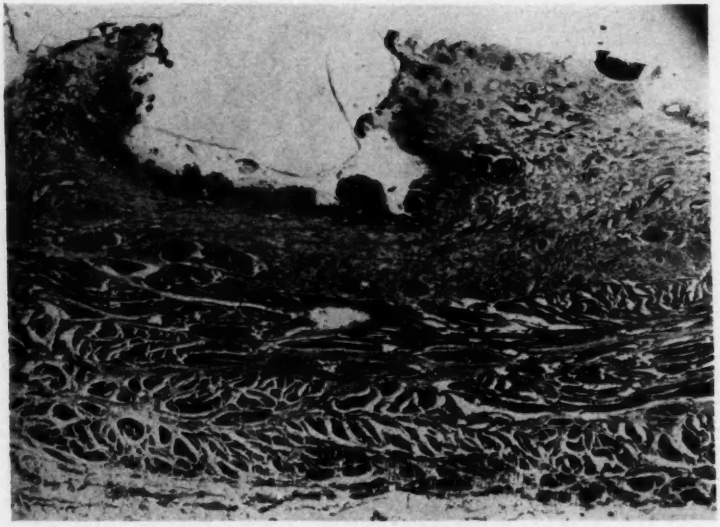


Fig. 4. Deep ulcer. Marked fibrosis.

effect upon the lesions in the urinary bladder. Marked improvement may gradually follow the interruption of the bacilli laden urinary stream which is constantly coming into the bladder. This may be accomplished by the surgical extirpation of the kidney, or ureteral occlusion resulting in autonephrectomy. Following nephrectomy the residual lower ureteral stump which is grossly involved with tuberculosis has long been recognized as a focus which may continue infection of the bladder. Unfortunately, however, interruption of the urinary current from the kidney to the bladder with its load of bacteria is not always followed immediately by alleviation of symptoms. Improvement occurs slowly over the succeeding

period of months or years as the tuberculous process is gradually smothered out. We realize that the patient who is relieved of his primary focus, but who may continue with his secondary lesions, is neither satisfied nor thoroughly treated. We have attempted by

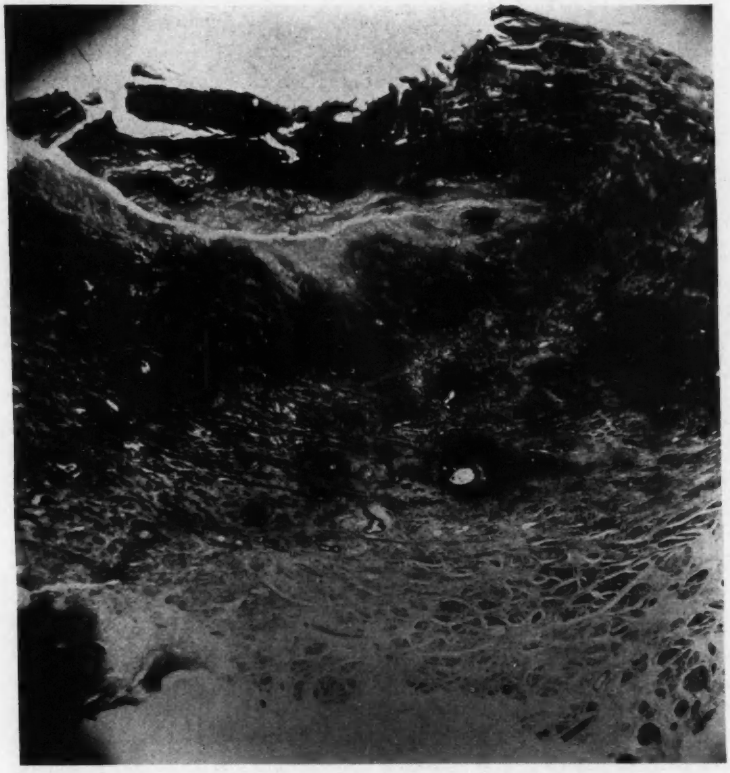


Fig. 5. Necrosis of the bladder wall with tubercles.

all known methods of treatment to bring about relief of bladder symptoms not only in the patients who have had surgical treatment, but also in those who are unsuited for surgery because of bilateral pathology or other adequate reasons. The methods we have used are, bed rest, control of fluid intake, diet with avoid-

ance of irritating foods, heat, irrigations of all types, avoidance of trauma, heliotherapy, local actinotherapy, splinting of the bladder and diathermy.

PRESENT METHODS OF TREATMENT

The first treatment we prescribe for patients who have tuberculosis of the bladder is complete bed rest. They are treated just the same as all other patients with other active lesions of tuberculosis. In certain instances we have tried splinting of the bladder, which was described by Keyes many years ago. By this means, particularly in the female, the bladder may be kept comfortably full and still comfortably empty, so that the patient does not stretch or hurt the ulcers as the bladder is being distended with urine and during the time the urine is being expelled. This method of temporary treatment has not been as successful in the male because of the difficulty in retaining the catheter in the urethra which may be infected.

Several years ago we became acquainted with the possible usefulness of light bipolar diathermy to control lesions of the bladder produced by tuberculosis. At this time this method was used to control severe bleeding from a tuberculous ulcer of the bladder. This patient had a nephrectomy elsewhere and was in our sanatorium because she had tuberculosis of the remaining kidney and tuberculous cystitis with ulcers. Her frequency of urination was improved somewhat during rest in bed but for a period of seven to ten days she had very severe bleeding which required some additional method of treatment to effect control. The ulcer, or the area which was bleeding in the bladder, was thoroughly coagulated by bipolar diathermy but a very weak current with low amperage was used. We were careful to produce a very superficial destruction of the inflamed, ulcerated area. This treatment not only controlled the bleeding but afforded the patient relief from much of her distressing frequency, burning and pain at urination. It was not very long before this patient requested that this treatment be given again because she had not only noticed that some of the bleeding had recurred but that her urination was easier following the treatment. The treatment was repeated and we not only cauterized the areas that were bleeding, but we coagulated every inflamed area in the bladder mucosa. Again the response from the patient

was favorable and three or four subsequent treatments were given. This patient's bladder capacity increased, her frequency decreased and she was rid of the very distressing trouble she had when attempting to urinate.

Following this experience we have used this method of treatment in a large number of patients with ulcers of the bladder that did not respond to the ordinary hygienic methods of treatment. To date every patient so treated has been relieved of his bladder symptoms, wholly or in part, especially when we were able to remove the lesion in the kidney that might continuously re-infect the bladder.

In addition to the relief of bladder symptoms in patients who have had a unilateral renal tuberculosis, we have had several experiences with the treatment of tuberculosis of the bladder in patients who have had a nephrectomy and still have tuberculosis in a remaining kidney. Rest in bed plus light coagulation of the inflammatory areas in the bladder has made these people more comfortable and in some instances the lesions have completely healed.

When this treatment is used in the male the urologist must be sure that there is no co-existing tuberculosis of the prostate or prostatic urethra. Infection here may continue the symptoms of frequency and painful urination with bladder ulcerations.

When ulcers of the bladder are treated with bipolar diathermy we advise spinal anesthesia. We are careful that the treatment is always under the direction of the eye. The electrode is not moved around the bladder recklessly. We must see its end at all times before the current is turned on so that the depth of the coagulation may be very carefully controlled. The examination of sections of a bladder that has been treated by diathermy suggests that the cautery tip should not be in contact with the bladder mucosa longer than one second in any one place. We limit the length of each treatment so that we may not cover all the ulcerated areas during one session. Subsequent treatments are given not earlier than fourteen days after the previous treatment. This method of treatment of tuberculosis of the urinary bladder has, in our experience, given more relief than any other method that we have tried.

CYSTOSCOPIC TECHNIC NECESSARY FOR THE DIAGNOSIS OF GENITO-URINARY TUBERCULOSIS

GILBERT J. THOMAS, M.D., and (by invitation) THOMAS J. KINSELLA, M.D., and CHARLOTTE C. VAN WINKLE, M.D.

Minneapolis, Minnesota

The presentation of a paper on the technic of cystoscopy has not attracted the attention of this society for many years. Our only reason for again calling your attention to this didactic subject is to point out that the ordinary cystoscopic technic as now practiced may not be adequate or exact when the diagnosis of genito-urinary tuberculosis is undertaken. It may not uncover all the data necessary for a complete diagnosis and may give misleading information. During the fifteen years that we have been especially interested in genito-urinary tuberculosis we have found it necessary to change the technic of our cystoscopic examinations many times.

An intimate association with physicians who are trained diagnosticians and therapeutists, and an opportunity to observe patients suffering from various lesions of this disease, have taught us that tuberculous individuals must be handled more carefully than others who are ill. This careful cystoscopic technic has been so satisfying to us in the diagnosis of genito-urinary tuberculosis that we have adopted it in our general work.

ANESTHESIA

We believe that thorough and complete anesthesia is necessary with patients who have any lesion of tuberculosis and who must submit to cystoscopic examination. This is particularly true of male patients. Before their examination is started we try to find tuberculosis of the posterior urethra, prostate or seminal vesicles. If lesions are present here it is very difficult and sometimes impossible to obtain the local anesthetic effect necessary with the usual methods now in vogue. If local anesthesia is unsatisfactory, and a general anesthetic seems necessary, we advise spinal or epidural infiltration, which offers the additional advantage of complete relaxation and lessened trauma to the bladder mucosa.

PREPARATION OF INSTRUMENTS

The urologist must be sure that his instruments are sterilized or thoroughly disinfected so that they do not harbor infection. Parts of cystoscopes that have no lenses may be boiled. If this is not possible they may be immersed in pure carbolic acid and washed in alcohol and sterile water, or they may be thoroughly washed in soap and water and placed in a solution of formalin or

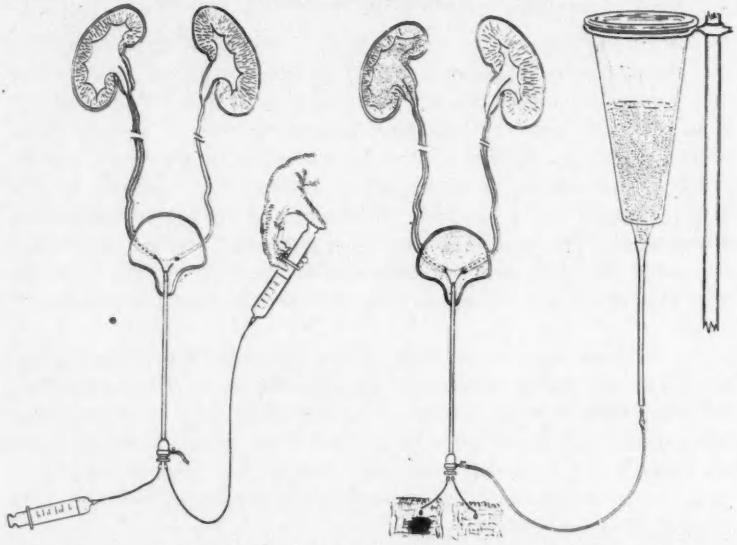


Fig. 1. *(left)* Method used to prevent contamination of interior of catheter during its introduction into the renal pelvis.
Fig. 2. (*right*) Ureteral reflex has occurred on one side.

oxycyanide of mercury. Frequent cultures of these solutions and of wash water after the instruments have been immersed in them produces sterile culture, so that the methods of sterilization of instruments herein suggested seem satisfactory.

The preparation of ureteral catheters is important. We have used the following technic, which disinfects and possibly sterilizes the catheter so that the urologist may be sure when it is introduced into the ureter that it does not contain tubercle bacilli or other pathogenic organisms. The catheters are carefully washed both inside and out with soap and water. They are then siphoned with

1-10,000 bichloride of mercury solution and eventually with sterile water for at least twelve hours. They may be stored in sterile towels after drying. Just before the catheters are to be used they are filled and then boiled for three minutes in distilled water. They are then immersed in a basin containing sterile water until they are used. Sterile water rather than an antiseptic solution is used here because the latter, when in the lumen of the catheter, may get into the culture tube and inhibit bacterial growth. Thus many negative urine cultures that might be positive are produced. After their use the catheters are cared for immediately; *i.e.*, the soap and water washing is done and siphonage started. This immediate mechanical cleansing and siphonage of ureteral catheters may be sufficient to disinfect them. Cultures after sterile water siphonage for twelve hours are usually negative. The efficiency of this technic has been proved bacteriologically by repeated tests using both tubercle bacilli and secondary organisms. After the instruments and catheters that are used during a cystoscopy have been carefully prepared so that we are sure they are uncontaminated with organisms that may infect the patient, we proceed with the preparation of the examiner and assistants. This preparation for a cystoscopy is just as complete and thorough as that used before laparotomy. We insist on the use of rubber gloves. The table set up by the nurse is just as carefully prepared as for any abdominal operation. The external genitalia of the patient are cleansed with soap and water and then with alcohol or some antiseptic solution. We use the usual light drapes over the patient's legs and abdomen and a special drape, about 4 feet square, which is put over the suprapubic area. This has a small slit in the center which permits the cystoscope and the penis to come through this small opening. Around the cystoscope this drape may be snugly held with clamps. This permits the urologist to manipulate the ureteral catheters through the cystoscope without contaminating them by contact with unsterile surfaces. Before the cystoscope is passed it is thoroughly lubricated. In the male a lubricant containing some antiseptic and an anesthetic is introduced with a syringe through the urethra and into the bladder. This permits the easy passage of the instrument with a minimum of trauma to the urethra. After the cystoscope has been passed into the bladder a sterile specimen of urine is obtained through it. This is used for microscopic study and guinea pig inoculation.

The irrigating fluid which is allowed to distend the bladder is always sterile. It may be either half saturated boric or plain sterile water. After the sterile specimen of urine has been obtained the direct vision cystoscope which we are in the habit of using is withdrawn sufficiently so that the prostatic urethra may be inspected. Here we are anxious to observe the character of the prostatic ducts and any other pathology which may be present. Since the careful examination of the prostatic urethra has become a routine part of our inspection we have found evidence of tuberculous infection in the prostate more frequently than previously. This has occasionally occurred in patients whose history and physical findings have not suggested the probability of tuberculosis of the prostate.

Following the inspection of the posterior urethra the bladder is carefully examined and the character of the ureteral orifices is noted. Although meatoscopy may reveal findings around one meatus suggestive of tuberculous renal infection on that side, this is not a constant observation in early renal infection. A tuberculous lesion of the kidney may be present and no evidence of inflammation may be found around the ureteral meatus on the same side or elsewhere in the bladder. We have observed areas of inflammation and ulceration distant from the ureteral meatus which expelled urine containing tubercle bacilli.

After a careful inspection of the bladder is made the ureteral catheters are introduced into the catheter guide of the cystoscope. To the outer end of each ureteral catheter, adapters with 20 c.c. glass syringes containing sterile distilled water are attached. The catheters are then continuously flushed with this solution before and during their passage through the catheter guide, the cystoscope, bladder and ureter. This is done to prevent contamination of the interior of the catheter by bladder urine. The first specimen of water or urine that comes through the ureteral catheter is discarded. After a free flow of urine is established through each catheter a strong solution of methyl blue is added to the dilating fluid and the bladder over-distended with it. This is continued until the patient complains of bladder over-distention and an intense desire to urinate. All of this time the urine which flows through the ureteral catheters is carefully watched for evidence of the return of the methylene blue. When this is obtained we know that reflux has

occurred from the bladder up the ureteral lumen to the renal pelvis and back through the ureteral catheter. When reflux occurs we properly evaluate the urinalysis of each ureteral specimen. Reflux has been demonstrated by this method in 16.5 per cent of our cystoscopies. This has occurred with all types of anesthesias and with or without evidence of tuberculosis or other pathology at the ureteral meatus.

Following the reflux test indigo carmine is given intravenously for estimation and comparison of the gross individual renal functions. Although we continue to use indigo carmine as a comparative functional test we know that minor differences in function do not necessarily indicate renal damage. Many observers refer to the differential dye test as one of the important diagnostic data which may indicate that nephrectomy should be done because of unilateral renal tuberculosis. We frequently find kidneys with large destroyed areas of tuberculosis that have no diminution of function. We have not been able to use the functional dye tests as positive diagnostic data unless confirmed by other findings. Following the differential functional test large specimens of urine are obtained through the ureteral catheters from each renal pelvis. These are used for microscopic study and guinea pig inoculation. We obtain not less than 10 c.c. and many times 20 c.c. are collected. These specimens are taken to the laboratory immediately. A cell count of each ureteral specimen is made at once and then they are centrifuged. The sediment obtained is divided and injected into two guinea pigs.

In our opinion bilateral pyelography is necessary before a diagnosis of the early renal lesions of tuberculosis can be made. Pyelograms will reveal the amount of renal destruction that has occurred and the character of the lesions present. We use two 20 c.c. syringes with close fitting adapters, and inject one renal pelvis at a time, but bilateral pyelograms are obtained on the same film. As soon as the roentgen exposure has been made and the film removed from the table the sodium iodide, or whatever material has been injected into the renal pelves, is aspirated into the syringes. This is done immediately following the making of the pyelogram, the amount which had been previously injected is carefully observed and this same amount is removed. The pyelogram is developed as soon as possible and if the pelvis is not well filled so that every calix and its ramifications may be distinctly seen the injection is repeated.

The film is developed and inspected immediately so that it may be examined before the patient leaves the table. Using this method we may save the patient a subsequent cystoscopy and we obtain complete information so that an exact diagnosis may be made.

Careful observation of patients with genito-urinary tuberculosis over a period of many years has demonstrated that aside from the occasional emergencies, as ureteral obstruction, pain, sepsis or hemorrhage, there is adequate time for complete repeated study of the patient and the genito-urinary tract. Intermittent excretion of tubercle bacilli from the kidney is the rule rather than the exception, therefore repeated examinations are required so that all possible and necessary data may be obtained. Renal tuberculosis, except in the occasional individual, is not a rapidly progressing lesion. The patient's chance for complete recovery is not reduced, but may even be enhanced by complete, thorough and repeated study prior to surgery.

We wish to suggest the following changes in the usual cystoscopic technic when patients are being examined for evidence of genito-urinary tuberculosis:

1. The use of anesthesia that will permit a painless cystoscopy, with minimum trauma.
2. Thorough disinfection of all instruments.
3. Proper sterilization of ureteral catheters.
4. Careful aseptic technic throughout the cystoscopic examination.
5. Careful inspection of the prostatic urethra.
6. Some method to prevent contamination of ureteral catheters during their passage to the renal pelvis.
7. Test for ureteral reflux and its evaluation when present.
8. Obtaining large specimens of ureteral urine for guinea pig inoculation.
9. Proper evaluation of differential functional tests obtained with indigo carmine or other dyes.
10. Bilateral pyelograms when not contra-indicated. Immediate inspection and retake if unsatisfactory.
11. Repeated urological study necessary before complete diagnosis is made and before radical treatment is undertaken.

DISCUSSION

DR. HUGH H. YOUNG (Baltimore, Md.): In my opinion, there has been entirely too much employment of suprapubic drainage in cases of prostatic obstruction. I have long been opposed to the two-stage operation, because, in the great majority of cases, urethral drainage is entirely satisfactory, and suprapubic cystostomy is certainly accompanied by a mortality that has been variously estimated from 2 to 4 per cent. By changing the urethral catheter every three to four days, and by frequent irrigation of the bladder and of the urethra when the catheter is removed, and reinserted after a few hours' rest, suppurative conditions in the urethra can usually be handled most satisfactorily. Where the infection is pronounced, or where hemorrhage and pain result from an inlying catheter, one can resort to intermittent catheterization; in fact, for a number of years I employed only intermittent catherization. While it is a little harder on the house staff, it is, I believe, one of the most satisfactory methods of preparing cases for operation, if catheterization happens not to be very difficult or painful. Cecil, who was my house officer at the time we employed intermittent rather than inlying catheterization, has continued to use the intermittent method almost exclusively, and his results are certainly among the best in the world, his mortality, if I remember correctly, being less than 3 per cent.

Another very effective and satisfactory method of vesical drainage is through an incision made into the bulbous urethra, under local novocain anesthesia. The urethra being larger, no difficulty is experienced in inserting a mushroom catheter. Good, dependent drainage, with much less urethral irritation, is obtained. One of the difficulties of catheter drainage is that occasionally the infection involves the prostate. This is hard to detect and I believe this is one of the serious dangers of suprapubic prostatectomy. After the prostate is enucleated suprapubically, the pus, which has invaded the prostate, remains in the cavity in which the lobes have been removed, with no adequate drainage, and sepsis results. With the perineal route, the incisions through the prostatic capsule effectively evacuate the pus, and give dependent drainage, as well as a chance to treat it antiseptically. In a recent case the prostatic infection

had extended up into the vesicles, which were also easily drained through the perineum.

Dr. Francis S. Watson (South Dartmouth, Mass.): I am glad to have the opportunity of expressing my agreement with what Dr. Young has said with reference to perineal drainage of the bladder. I have used it frequently in the past and have always found it of value in such conditions as those to which he referred.

Dr. Charles M. McKenna (Chicago, Ill.): I just want to make a few remarks concerning the ureteral stump after the removal of a tuberculous kidney. I think we all have seen cases with persistent fistula following the removal of a tuberculous kidney. This is usually due to the infected ureteral stump. A year ago I showed the value of doing an inversion of the ureteral stump when the ureter was patent and in this way turning the ureter outside in, doing away with the infected area's draining into the perinephric space. I will not go into that inasmuch as it is published elsewhere. I would like to ask Dr. Thomas what results he has had by using the mirror to reflect the light into the open bladder in patients suffering with tuberculosis of the bladder.

Dr. William E. Lower (Cleveland, Ohio): I have been rather surprised that there has not been more universal use of the suprapubic drain by trocar and cannula. This can be easily and quickly done under local anesthesia. If the bladder is not distended with urine, then it should be filled with some solution so that it will be well outlined. The trocar and cannula are inserted, the trocar is removed, and through the cannula a catheter is introduceed. The cannula is then withdrawn over the catheter, and the catheter allowed to remain as a drain. This can easily be held in place and does not cause the patient any discomfort. A small stopper is inserted into the end of the catheter and the patient can readily get about, draining his bladder whenever he feels the urge. In this way it is possible to drain behind the enlarged prostate, a very difficult thing to do by perineal incision. It is easy to do, the material is readily sterilized by boiling, and there should be no hemorrhage. This drainage can be continued for such length of time as may seem necessary to work out the problem of permanent relief. It is quite important that the cannula be of such size that the catheter

will readily pass into it. We have such a one constructed, which will take a No. 16 catheter, and another which will take a No. 18 catheter. This we consider the most important equipment we have to meet emergencies of acute urethral obstruction.

DR. J. DELLINGER BARNEY (Boston, Mass.): I, too, have been interested in the subject of perineal drainage in cases not only of prostatics, but also in cases where the penis is amputated or where there is hypospadias or epispadias, or any operation where the urinary stream should be diverted. In 1918, I published the results and the description of an operation which I had then been using for some years. The second installment of that publication is coming out in a future edition of *Surgery, Gynecology and Obstetrics,* and it is fully as simple as Dr. Young's. I am not sure that it is not even a little more simple. I don't know that I can draw it in sixty seconds, as Dr. Watson described what could be done in sixty seconds, but if this is the urethra (illustrating on the blackboard), one simply takes an ordinary soft rubber catheter and puts it into the bladder as far as it will go, until the end of the catheter is about at this point, just outside the meatus. Then you grasp that end of the catheter with a clamp and continue right on with the clamp and the catheter until the clamp with the catheter in it is right here (in the bulbous urethra). Then you turn the point of the clamp about, so the skin is somewhat bulging on the end of the clamp, and then you can put in a drop or two of novocain and make an incision just wide enough to get the clamp out. So when you get the clamp out, there is the end of the clamp and the catheter. You grasp the catheter with another clamp, undo this clamp and pull it out, adjust the catheter, take two sutures there to close the wound and control hemorrhage and to hold the catheter in place.

I have done that three and four times in different cases at intervals of months or years. There was no stricture formation, and no more difficulty in doing it for the second time or third time than there was the first time. The patient can get up and be around. It is the speediest method I know that can be done with the patient flat on the table, with the legs somewhat separated.

DR. F. R. HAGNER (Washington, D. C.): I had not intended to say anything today because I thought there would be a great deal of discussion. In using the bag following prostatectomy we have

occasionally had a patient who bled after putting the bag in. To overcome this, we have a little handkerchief made about that size (illustrating) with one opening in the center. The bag goes through the opening, and that is pulled down in the bladder over the bag and the bag is then blown up. This has not failed to control the bleeding.

For many years we have occasionally attached a piece of silk suture to the tube of the bag. This is pulled through the urethra with one end left out of the suprapubic wound and the other end out of the urethra. If hemorrhage does occur we tie the piece of silk that protrudes from the bladder to the end of the bag and pull it back into place without putting an instrument in.

DR. NATHANIEL P. RATHBUN (Brooklyn, N. Y.): Of course, there are a number of cases that won't tolerate an indwelling catheter, and in those cases, inasmuch as I do most of my prostatectomies by a two-stage suprapubic method, I am rather inclined to do promptly a suprapubic cystotomy, although I have frequently used the method Dr. Lower speaks of, the trocar and cannula. That is a very valuable method in emergencies, not only in prostatic cases, but in urethral strictures that have been traumatized and badly handled before admission of the patient to the hospital.

About the drainage Dr. Young suggests: I hesitate, of course, to find fault with anything that such eminent authorities as Dr. Young and Dr. Watson present and assume, perhaps *a priori*, I must be wrong because I am finding fault with them, but the fact remains drainage of the bladder by this method does involve the presence of a foreign body in the prostatic urethra, and it seems to me that is not good surgery when you are going to operate the prostate a little later.

DR. GILBERT J. THOMAS (Minneapolis, Minn.): Just a word about the sterilization of ureteral catheters. Many urologists put their ureteral catheters into a disinfecting solution, and then introduce them into the ureters. At once they begin to collect urine on culture media. We have tried this method, and find that, if the antiseptic solution is strong enough to be a disinfectant, a drop or two washed through the catheter and into the culture tube will prevent the growth of bacteria.

PRESIDENT CAULK: Dr. Young wants to ask Dr. Rathbun a question.

DR. HUGH H. YOUNG: Dr. Rathbun objects to that catheter being in the urethra about 3 inches in length because it is a foreign body. Do you treat any patients in a preliminary way before prostatectomy with an inlying urethral catheter?

DR. RATHBUN: Inasmuch as I do most of mine by the two-stage method, there is a period between the period of inlying catheter and the period of the prostatectomy.

DR. YOUNG: Well, I suppose it is safe to say about 90 per cent of the prostates are prepared for prostatectomy by an inlying urethral catheter. I don't believe people have found an inlying catheter very bad on the prostate when they operated on it.

STATE OF UNILATERAL ANURIA IN BLADDER MALIGNANCY

ALEXANDER RANDALL, M.D., F.A.C.S.
Philadelphia, Pennsylvania

In 1927 this Association had the privilege of hearing the late Dr. Arthur L. Chute draw attention to the death of patients from renal insufficiency in advancing carcinoma of the bladder. Dr. Chute entitled his paper, "The Part that Obstruction of the Ureter Plays in the Outcome of Cancer of the Bladder." He had observed fourteen autopsies on cases of bladder malignancy, and stated: "The main point of interest is this, that in these fourteen autopsies we found twelve cases in which a ureter was more or less dilated due to compression by disease; in four of these instances both ureters were dilated." It was through this communication that our attention, I believe, was first accurately focused on the occurrence of an obstructive uropathy with uremic death in patients suffering from bladder malignancy. Chute continues by saying: "These findings suggest to me that dilatation of the ureters may be a pretty general occurrence in cases of carcinoma of the bladder and account for a considerable element of the mortality in these cases." In this communication, as well as in two others, Chute accentuates the finding of ureteral dilatation and discusses the part played by the malignancy in causing this dilatation by obstruction to normal ureteral function. I believe we have accepted the finding as a most pertinent clinical observation, and a simple example of an obstructive uropathy with concomitant hydro-ureters, hydronephrosis and increasing renal insufficiency.

Our general knowledge of ureteral and renal pelvic function fits into this picture. We know and expect with sudden complete blockage (such as ligation of one ureter) an acute increase of pelvic pressure and, in the absence of infection, a rather prompt unilateral secession of renal function, while in contradistinction a gradually developing blockage is uniformly accompanied by first an hypertrophy and later a constantly increasing hyronephrotic dilatation. Certain it is that any obstruction arising from a malignant bladder growth would belong to the latter group of gradually developing

blockage and find its corollary in the picture so well described by Chute and generally recognized in other partially obstructive conditions. There certainly is no reason to expect that a bladder tumor would cause, at any time, sudden and complete occlusion and be comparable to a ureteral ligation.

Since the introduction of intravenous urography, I have been studying early cases of malignant bladder tumor by this method, in an effort to appraise the proper cases for ureteral transplantations and total cystectomy. In the past two years out of fifty-nine cases of bladder malignancy we have studied fifteen cases of particularly localized tumor by intravenous urography. While four of these fifteen cases have evidenced normal bilateral function, and four others varying degrees of hydronephrosis, as depicted by Chute, seven cases have surprised us with pictures of apparently unilateral non-functioning kidneys. In each of these seven cases the urograms have shown on one side a shadow of an apparently normal renal outline but, in no plate, the slightest evidence of excretory function therefrom. In each of these seven cases the dead kidney is on the same side as the evident bladder growth, and one cannot separate the obvious relationship between tumor, ureteral involvement and the unilateral failure of renal function. In each of these cases this renal death has been silent, entirely symptomless and totally unsuspected. The one outstanding fact has been the apparent total absence of evidence of hydronephrosis, even in the plates taken three and up to five hours after injection, and one begins to think, not of a disuse atrophy, but of a silent renal death, or a unilateral reflex anuria. These patients have not shown any symptoms of renal embarrassment and have not evidenced an elevated blood chemistry.

COMMENT

One can theorize along several lines to account for these findings:

1. There certainly is no reason to expect a sudden and complete occlusion that would allow this condition to be compared with ureteral ligation or complete stone blockage.

2. In the absence of infection it should be to a degree comparable with partial stone obstruction or pregnancy, but the parallelism stops here, for in these latter conditions marked hydronephrosis is outstanding.

3. From the study of our films the kidney shadow appears quite normal, and the frequency of the occurrence as observed in these seven cases rules out chance pathology.

One turns naturally to seek an explanation in other bodily functions where somewhat comparable conditions are recognized to exist, and there comes to mind the frequency of pylorospasm in appendiceal irritation and in hyperchlorhydria; likewise the negative gall-bladder function in duodenal ulcer; and we like to think of this unilateral suspended uropoiesis as perhaps a protective reflex where, with one unhampered kidney to carry on the required bodily work, its embarrassed mate ceases to function.

In substantiation of this theory we have cases where the malignant growth covered the bladder base to an extent that unquestionably involved both ureters. In these cases differing degrees of bilateral hydro-ureters have been present, evidencing the fact that, when vital renal function is truly embarrassed, the bodily response is quite different, for then a fight is on which calls forth the utmost compensatory function and fails only after marked hydronephrotic destruction has transpired.

BIBLIOGRAPHY

1. CHUTE, A. L.: The part that obstruction of the ureter plays in the outcome of cancer of the bladder. Trans. Amer. Assoc. G.-U. Surg., 20:295, 1927.
2. CHUTE, A. L.: Am. Jour. Urol., 19:577, 1928.
3. CHUTE, A. L.: Ureteral transplantations in bladder carcinoma. Jour. Am. Med. Assn., 87:1613, 1926.

METASTASIS IN EPITHELIOMA OF THE URINARY BLADDER*

A. DWIGHT SPOONER, M.D. (by invitation)
From the Department of Urology,
The Mayo Foundation, Rochester, Minnesota

A review of the literature of the past twenty years concerning tumors of the bladder reveals a vague but fairly unanimous clinical opinion on the subject of metastasis. It is commonly stated that tumors of the bladder do not metastasize, that they metastasize infrequently, or that they occasionally metastasize late in the disease.

Authors of textbooks on urology, surgery, or pathology dismiss the subject with a brief sentence or paragraph in which they repeat the opinion of predecessors or report one or more cases encountered in their personal experience. With one or two exceptions they either ignore or briefly allude to metastasis as being of infrequent occurrence.

The literature from 1828 to 1881 is practically limited to scattered reports of cases in which metastasis took place; historical review of this literature is scarcely worth while. Since 1881, Féré, Albarran, Pasteau, Grandjean, and Cunningham have contributed the outstanding and interesting studies.

As late as 1918, Geraghty wrote:

"It is usually noted that the bladder tumors, except in comparatively rare instances, remain well confined to the bladder cavity and do not tend to invade the surrounding structure; nevertheless, metastasis to distant points is not infrequent. There are no convincing statistics regarding the frequency of glandular metastasis. It is generally admitted that when the tumor is extensive, infiltrates deeply the bladder wall, that metastasis is practically always present. When, however, the tumor is comparatively small, and only slightly infiltrating, we have no definite statistics as regards frequency of metastasis. That the tumor may be occasionally very extensive, and even deeply infiltrating, without metastasis, has come under our personal observation. . . . On the other hand, metastasis may occur in malignant papilloma in which there is present not the slightest evidence of infiltration of the bladder wall. Metastasis to the bones seems to be quite frequent. . . . Metastasis to

*Abstract of thesis submitted to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Urology.

the vertebræ is not infrequent. The lungs, liver, and spleen are favorite sites for metastatic processes."

Keyes, in 1928, wrote:

"The incredible advance that has occurred in the curability of bladder tumors of late years is due to radiotherapy but is made possible by the slowness with which these tumors spread, either by metastasis, or direct extension."

Any considerable number of cases in which there are metastatic lesions from malignant growths of the bladder usually are collected from studies made at necropsy. Such cases, however, are regarded by many observers as examples only of what occurs when the disease is protracted; that is, they are examples of the end-result in the few cases in which the patient dies after harboring the disease for many months or many years.

On the other hand, in any large clinic or hospital in which diagnosis and treatment of tumors of the bladder is carried on, a considerable number of fatalities is certain, and the complications following surgical intervention are more or less important contributory causes of death. Among these cases will be those in which the duration of the disease was brief and apparently uncomplicated by metastasis. If, however, a considerable number of the patients who die after a short illness reveal metastasis at postmortem examination, the incidence of metastasis should be important as a fairly reliable index of the metastatic lesions to be expected in similar groups of cases in which the condition is considered operable.

Metastasis from tumor of the bladder is seldom encountered by surgeons. From the time of the earliest surgical intervention for tumor of the urinary bladder, when the lesion was snared out or curetted through a divulsed urethral sphincter, through a later era when the perineal boutonniere was popular, and down to the modern transurethral or transvesical and extraperitoneal approach, the surgeon rarely has had access to the more common regions of metastatic involvement.

In this age, removal of carcinoma of the cervix, labia, penis, lip, breast, or stomach, without regard to regional or distant metastasis, is almost unheard of. Yet in the modern treatment of tumors of the bladder, often the principle which is applied when dealing with carcinoma elsewhere in the body is ignored. Accordingly, it seemed important to examine the histories, clinical records, operative and

pathologic reports, and the material obtained at necropsy in a fairly large series of cases, to determine the accuracy of the axiom that tumors of the bladder do not metastasize and to record the incidence and site of metastasis thus encountered.

MATERIAL

The materials used for this study were the clinical records, protocols of necropsy, and gross and microscopic pathologic specimens in all cases of tumor of the bladder in which examination was made at The Mayo Clinic from 1914 to 1931, inclusive. It should be stated that reference to tumors applies exclusively here to epitheliomas. The clinical records of all cases were tabulated in detail. The history, diagnosis, treatment, clinical course, clinical cause of death, and anatomic diagnosis were noted in each case. The presence or absence of metastasis was ultimately determined by the descriptions recorded in protocols of necropsy and verified by study of the microscopic sections. In a few instances in which microscopic proof was missing, fresh blocks were cut for this purpose, as well as to determine the type of growth (grade of malignancy).

Analysis.—In The Mayo Clinic, from 1914 to 1931 inclusive, postmortem examination was obtained in 163 cases of carcinoma of the bladder. Of the total number of patients, 116 came to operation for the condition of the bladder. Of those cases in which death resulted from complications, in many, at postmortem examination, it was found that the tumors of the bladder were in comparatively early stages. Metastasis occurred in forty-nine of the total number of 167 cases, or 29 per cent. Only four of these forty-nine patients presented sufficient clinical symptoms to enable a positive clinical diagnosis of metastasis from tumor to be made. The age limits for the forty-nine cases were from thirty to eighty-five years; the average age was fifty-seven and four-tenths years.

The symptoms in twenty-four of the forty-nine cases, approximately 50 per cent of the total, were less than two years in duration. Nineteen patients (38.9 per cent) had symptoms less than one year.

One or more distant viscera contained metastatic implants in twenty-four of the forty-nine cases, or 48.9 per cent of the cases in which metastasis was present. The extent of involvement in such instances varied from single nodules, a few millimeters in

diameter, to multiple implants ranging from a few millimeters in diameter to virtual destruction of the organ involved. The liver was the commonest seat of involvement, in fourteen cases. Following, in order of frequency, are the lung, suprarenal gland, and kidney. The heart was involved in as many cases as was the kidney. Other organs or tissues that were involved were the spleen, pancreas, thyroid gland, stomach, bones and peritoneum. It is interesting to observe that metastasis to distant viscera, without apparent involvement of lymph nodes, and without evidence of direct extension to adjacent tissue, occurred in six of the twenty-four cases in which visceral lesions were present. This does not accord with the statement frequently encountered in the literature to the effect that distant metastasis occurs only after adjacent structures and nodes are involved. No metastasis to the brain was encountered in this study, but examination of the head was performed only in those cases in which suggestive neurologic symptoms were presented. The low incidence of skeletal involvement appears to bear out the opinion frequently expressed, that invasion of bone, except by direct extension, is an uncommon feature of metastasis from tumors of the bladder.

In the total of forty-nine patients who presented metastasis, the lymph nodes were involved in thirty-four instances, or 69 per cent. This number includes many cases in which there was distant metastasis as well, and represents 20.8 per cent of all the cases of tumor of the bladder in which portmortem examination was performed. Metastatic involvement was found to be strictly confined to lymph nodes in only twelve of the thirty-four cases in which lymph nodes were involved. Unfortunately, information as to the exact situation of the nodes involved was lacking in several protocols, and in the corresponding cases the words "regional" and "pelvic" had to be accepted as descriptive of the situation. In detail, the lymph nodes involved, and the number of cases in which they were involved, were as follows: regional, ten cases; iliac, five; iliac and aortic, two; iliac and lumbar, two; pelvic, three; lumbar, one; retroperitoneal, one; perivesical, one; inguinal, two; inguinal and hilar, one; aortic, four; aortic and mediastinal, one; and sacral, one. Moreover, in one case there was carcinomatosis of the lymphatic system.

Adenocarcinoma was encountered in two cases; in the remainder,

the growths were squamous-cell epitheliomas. It is to be noted that in all but five instances the grade of malignancy of the growths in these forty-nine cases was 3 or 4 (Table I). A marked preponderance of higher grades of malignancy (Grades 3 and 4) substantiates the contention that a malignant growth can accomplish only what its cells can accomplish, and that the more malignant the histologic type of growth, the more likely is it that the lesion will grow rapidly, extend, and metastasize. Conversely, it is implied that growths of malignancy graded 1 and 2 (benign papillomas so-called by many authors) extend less rapidly, if at all, and show less

TABLE I. GRADE OF MALIGNANCY AND DURATION OF SYMPTOMS

Grade	Cases	Duration of symptoms, years	Comment
4 3 2	16 23 5		
	1	16	Induration felt per rectum
	2	2	Induration felt per rectum
	3	8	Extensive lesion per cystoscopy
	4	4	Extensive lesion per cystoscopy
	5	1.5	Extensive degenerating lesion per cystoscopy

tendency to metastasize. Five cases, however, in which malignancy was of Grade 2, were exceptions to the implied hypothesis, for involvement of lymph nodes was present.

In twenty-seven of the forty-nine cases, operation was performed; in five cases, operation was performed and radium was applied; in three cases, the only treatment was application of radium; in one case, only roentgen therapy was given, and in one, fulguration was performed and radium was applied. Thus, thirty-two of the forty-nine patients were surgically treated. Surgical intervention was doubtless a palliative measure in some of these cases. In many, however, the lesion had not extended beyond the wall of the bladder, as far as clinical methods could determine, and hence was considered amenable to cure by surgical operation. This is pointed out to show that this paper does not deal exclu-

sively with far advanced, inoperable cases of carcinoma of the bladder.

Although the existence of metastasis was surmised in many cases of carcinoma of the bladder, nevertheless the records show that it was recognized clinically in comparatively few cases. The clinical data were reviewed, therefore, for information which might reasonably be called suggestive of extravesical extension. On rectal examination, perivesical infiltration was found in eight cases and unilateral prostatic or vesical infiltration in six. An extensive lesion was evident on cystoscopy in twenty cases. In thirteen cases, pain was present. Symptoms were of long duration in eleven cases, and malignancy was of Grade 3 or 4 in thirty-nine cases. The foregoing enumeration would suggest that metastasis was surmised in many instances. However, in several cases, although some of the symptoms and signs named were present, there was no evidence of metastasis. In many cases, on the other hand, although none of the signs and symptoms named were present, widespread metastasis existed.

COMMENT

Three factors appear to have influenced previous conceptions of metastasis from tumors of the bladder. The first is the paucity of published reports of cases. Until 1898 reports of proved cases were largely confined to reports of necropsy in cases of long standing, not many of which were encountered in the experience of one individual. The second factor, which appeared to correspond with the experience of individuals, was the belief promulgated by anatomists such as Sappey, that the bladder did not possess lymphatic structures; hence, the usual channels for extension of carcinoma were wanting. The third factor has been the infrequency with which metastasis could be clinically demonstrated, especially by roentgen rays, in comparison with malignant growths of the prostate gland and kidney.

The former belief that metastasis from carcinoma of the bladder rarely takes place has been perpetuated by the infrequency with which clinical evidence of metastasis has been found. Since skeletal metastasis is not a prominent feature, reliance on roentgen rays has been relatively less satisfactory in diagnosis, as compared with prostatic carcinoma. To the average clinician, therefore, metastasis

in carcinoma of the bladder has been, and likely will continue to be, a matter of conjecture.

A survey of the grade of malignancy of the tumors concerned in the study here reported verifies the practicability and accuracy of Broders' classification of tumors of the bladder and its clinical application, as suggested by Braasch and Crenshaw; namely, that growths, of malignancy graded 1 and 2, if not too extensive, can be treated properly transurethrally by fulguration, whereas growths of malignancy graded 3 and 4, in most cases are probably better treated by transvesical methods.

The marked disparity in figures concerning the incidence of metastasis of carcinoma, obtained from studies made at necropsy, is striking. It has been seen that, among cases in which search for metastasis has been made by the pathologist, a surprisingly high percentage of cases has been found in which metastasis has taken place (Pasteau, 79 per cent). In a series of cases studied at postmortem examination, such as the series collected by Cunningham, metastasis was found in 32.3 per cent of 411 cases. In the present study, the incidence was 29 per cent.

Doubt may be fairly expressed as to the thoroughness of the search for metastasis in the average case of carcinoma of the bladder in which necropsy is performed. It is obvious that gross lesions would be detected, but unless careful search through the adipose and areolar tissue of the iliac and hypogastric grooves is made, an early lesion readily could pass unobserved. In the study reported here, the cases date back to 1914, and although a thorough search was assumed to have been made in all cases, we have positive assurance that such study was made only in relatively recent years.

Since the difficulties of clinical detection of metastasis are apparent, one would naturally turn to the surgeon for information to substantiate or disprove the pathologist's figures. But here a fact regarding current surgical practice is encountered. Except in instances in which segmental resection, with extirpation of homolateral lymph nodes is practiced, and those instances in which the peritoneum is opened to resect an involved portion, the surgical approach generally employed provides inadequate exposure for exploration or detection of either regional nodes or of distant visceral involvement. Surgical opinion based on such practice should not be the sole basis for an opinion regarding metastasis.

The modern surgical attack on carcinoma of an organ is importantly concerned with the search for, and removal of, the associated lymph nodes, with the striking exception of operation for carcinoma of the bladder.

Whether preliminary exploration to determine evidence of metastasis would be a justifiable procedure, or whether removal of iliac nodes can be readily accomplished, may be matters which surgical authorities would question. It is suggested, however, that if more accurate information concerning metastasis can be obtained at operation by exploring the abdominal viscera (especially the liver) and the pelvic and pre-aortic lymph nodes, without substantially increasing the risk to the patient, many radical operations which are undertaken in the hope of obtaining cure might, as a result of the discovery of important metastatic deposits, be converted into palliative procedures entailing less surgical risk and maintaining equally satisfactory end-results.

Of the cases concerned in the present study, in 29 per cent of all in which postmortem examination was performed metastasis was found. Thirty-two of the forty-nine were surgical cases. In many of them there was possibility of surgical cure.

SUMMARY

Of 163 proved cases of tumor of the bladder in which postmortem examination was performed, in forty-nine, or 29 per cent, metastasis was found. Of the patients who had metastatic lesions, 65 per cent were regarded as amenable to surgical treatment; many of these had a chance of surgical cure as far as clinical judgment could determine. The commonest site of malignant extension is the regional lymph nodes. They were involved in thirty-four of forty-nine cases in which metastasis was present, or 69 per cent. Lymph nodes represented the only apparent site of metastasis in twelve (24.4 per cent) of the cases in which metastasis was present. Metastatic growths were found in one or more distant viscera in twenty-four instances (48.9 per cent) of the entire group of cases in which metastasis was found. The liver was involved in fourteen cases and the lung in nine cases, to represent the more commonly involved viscera. Skeletal involvement is an uncommon feature of metastasis of tumor of the bladder. Estimation of the incidence of metastasis of tumor of the bladder, based on many surgical studies,

may be inaccurate because exploration for metastasis was not made. Clinical data, presumably indicative of extravesical extension, are often furnished by rectal examination (perivesical induration), elicitation of a long history, determination of a large lesion cystoscopically, disclosure by biopsy of a lesion, of malignancy graded 3 or 4, and the presence of persistent pain unexplained by the local lesion. Of the 163 patients concerned in the present study, 29 per cent had metastatic lesions which in many cases had been unsuspected clinically.

DISCUSSION

DR. JOHN H. CUNNINGHAM (Boston, Mass.): This paper interests me very much as it is a subject that I have attempted to get data on over a long period of time. I have collected 411 protocols of malignant tumors of the bladder in which 133, or 32.36 per cent, had gross metastases. Dr. Spooner's series is 29 per cent. So we are not very far apart.

There should be no objection, I believe, in assuming that these metastases are relatively common simply because they are observations of end-results. The metastases are there, they are gross, and I see no reason to believe that they don't take place during perhaps earlier stages in the disease than we believe. While I am certain that most of my patients have died from kidney disease and other causes, I am equally positive that many of these patients have had metastases, and I believe the metastases have been quite an important factor in the termination of the life of many of them.

As the reader has said, he believes as I do, there is a false impression in regard to the frequency of metastases in malignant tumors of the bladder. The attitude that he assumes I agree with entirely. I think we will have to change our point of view about tumors of the bladder metastasizing seldom, and late when they do occur. I believe it is quite the contrary, and I am delighted that Dr. Spooner's figures substantiate this belief.

DR. ARTHUR B. CECIL (Los Angeles, Calif.): I was very much interested in Dr. Randall's paper in which there was cited an instance of failure to excrete pyelographic media on account of blockage of the vesical end of the ureter by a bladder tumor. I take it that it is his belief that the blockage of the ureter was the reason for failure to get a picture. I think it is not at all uncommon to see a stone in the ureter produce just that same type of thing where one gets a picture on one side and absence of picture on the other. Of course, I understand that that is, as a rule, a more or less acute process, but tumor blockage may be so and I do not believe that one can predict absolute renal death simply because one fails to get a picture. A nephrostomy may or may not restore the kidney. It has been my experience that where a kidney is blocked by a bladder

tumor that destruction of this tumor by diathermy or heat is a very dangerous thing unless a nephrostomy is first done on that side. I have seen two deaths follow in this type of case from ascending renal infection confirmed by autopsy.

DR. WILLIAM F. BRAASCH (Rochester, Minn.): I have been very much interested in the condition described by Dr. Randall, and have observed a number of patients in whom excretory urography showed an absence of visualization of a kidney which apparently was blocked by bladder tumor.

In several cases of this type Dr. Counseller of our staff has resected the neoplasm, freed the involved ureter, and, after introducing a No. 16 catheter into it, drained it through the urethra, with coincident suprapubic drainage. The independent drainage gave us an opportunity to study the secretion of these kidneys, both before and after operation. Excretory urography made routinely in all patients with bladder neoplasm frequently demonstrates evidence of diminished renal function in one or both kidneys. When the neoplasm involves a ureteral orifice the visualization of the affected kidney is usually reduced and in many cases absent. On the other hand, there may be no evidence of reduced renal function in spite of involvement of the entire base of the bladder. It is evident that abnormal function is dependent on the degree of renal back pressure. After the neoplasm has been removed, if no damage has been done the ureter, the renal function will in many cases return, in the course of two or three weeks after operation. In other cases it will not return until two or three months later. In some cases, however, the injury to the kidney has been permanent, and the kidney remains functionless.

It would seem probable that some of these cases would substantiate the contention made by Dr. Hinman that function of a kidney which is temporarily rendered functionless sometimes fails to return when the other kidney has assumed the combined renal function for a period of time. In some of the patients observed the function of the kidney involved was irreparably lost.

Dr. Randall's discussion as to the possible causes for the cessation of function are of great interest. The possibility of sudden occlusion of the ureter by the growth or edema of the bladder cannot be excluded. Ureterectasis to a variable degree, extending to

the wall of the bladder, would confirm the probability of obstruction. Dilatation of the ureter to a marked degree is often observed in the opposite side, although there is no possibility of obstruction from tumor. It is difficult to explain such ureterectasis, although in some cases ascending infection may be a factor.

Dr. Randall also brought out the fact that these patients may have no symptoms of abnormal renal function and yet retention tests will often show a blood urea well up in the forties. On the other hand, extreme elevations of blood urea are seldom noted with this type of obstruction, except with extensive involvement of the entire base of the bladder, and with terminal stages of the disease.

The frequency with which perivesical and distant metastasis occurs with tumor of the bladder has been graphically shown by Dr. Spooner. Although Dr. Cunningham and other observers have called attention to such metastasis, nevertheless there still remains a widespread impression that tumor in the bladder is not usually complicated by metastasis or only as a terminal lesion. From an unusually large number of cases checked up by autopsy reports and careful operative notes Dr. Spooner shows that metastasis may occur even with early lesions. He has shown that metastasis in most cases is largely confined to the lymph nodes adjacent to the bladder. This brings up the point whether it would not be feasible in these cases to explore the iliac lymph nodes and, if possible, remove such as are involved.

Dr. William C. Quinby (Boston, Mass.): Both these papers have been exceedingly interesting. I will speak first about Dr. Spooner's, on which I congratulate him heartily. It is a splendid study and appeals to me especially because it confirms what I have suspected without having had sufficient material to confirm my suspicions.

The matter of metastases interests me especially as it concerns the choice of patients for total cystectomy for cancer. I have been trying continuously to apply whichever of our various methods exists in the attack on cancer to the individual patient; not performing a total cystectomy, or not using radium, or not trying any other method for the sake of the method, but attempting to apply whatever method seemed most applicable to the conditions presented by each individual patient.

The standards which I have set up for myself in regard to the suitability of a patient for a total cystectomy have been, (1), an involvement of the floor of the bladder so wide that if that malignancy were to be locally treated by any method, such treatment would involve the outlet of the bladder to such an extent that there would result loss of vesical function and incontinence; (2), I have insisted that there be no demonstrable metastases outside the bladder, and I have gone so far in each case, before subjecting the patient to a total cystectomy, as to investigate the retroperitoneal drainage area from the bladder, as a preliminary step. I have been much discouraged in more instances than I cared to believe possible to find involvement of the pre-aortic lymph nodes, or of the lymphatic channels leading up from the pelvis to that region. Of course, the patient is further studied by ordinary x-ray methods or whatever other method we have at our command to demonstrate secondary deposits. But in those instances in which one opens the peritoneum and investigates the retroperitoneal regions, it is surprising to see how often one will find them already the site of secondary deposits. It is possible, I suppose, to treat these areas in a way similar to that by which surgery treats the axilla in cancer of the breast, namely by dissection, but this is a matter for the future. If it is possible to make a comprehensive dissection of these areas, then some good may be done. I am afraid, however, that this is rather imaginative.

I was also very much interested in Dr. Randall's communication because his experience again fits in with mine, although I would like to ask him his opinion in regard to the films following intravenous pyelography. I am not clear in my mind that the absence of filling of the renal pelvis by this method necessarily means death of the kidney. I believe that renal death is a gradual process and I don't believe that one is going to be able to say at any one moment in an individual case just how much that kidney is damaged. We know it is damaged severely, but whether it will recover or not, I don't believe any one of us can say.

Dr. Braasch says that this matter is being investigated now at his clinic and that the damage is considerable, but I am not sure that it is irreparable in all cases in which there is lack of filling by the intravenous drug.

DR. JOHN R. CAULK (St. Louis, Mo.): I am very much inter-

ested in Dr. Randall's paper. I am now in the process of studying some 500 cases of bladder neoplasms with reference to the fate of the upper urinary tract, which we know is usually precarious, and I have a few figures in which you might be interested. We have completed the study of 300 cases with reference to the renal involvement and find that the kidney may be involved in three ways: first, by simple regurgitation from incompetency of the ureteral valve disturbed by spread of the tumor invading the mucous membrane; second, by implication of the intramural ureter with stenosis; and, third, by extravesical occlusion of the ureter from gland involvement or superimposed inflammatory reactions around them.

In cases in which we were suspicious of invasion because the tumors were located close enough to the ureter possibly to invade it and to do damage to the kidney, we found in the cystographic studies that 24 per cent showed regurgitation; 50 per cent showed regurgitation without indentures of the wall of the bladder, in other words, without evidences, so far as we could tell, of mural invasion, and the other 50 per cent showed wall invasion. Seventy-eight per cent of the tumors were located around the trigonal neighborhood close to the ureteral orifices. One hundred forty-four patients were studied with reference to their functional renal capacity, that is by nitrogenous blood studies or excretory tests, particularly phthalein, and of these we found 44 per cent showed definite diminution of renal function; 21 per cent of all the 300 patients showed renal infection. There were ninety deaths, and of these ninety deaths, 38 per cent had positive evidences of upper urinary tract disease; twenty-five of these came to autopsy, and of these twenty-five patients, 60 per cent died a renal death, a tremendous renal mortality.

Now in extension of tumors to the bladder, particularly with reference to the carcinoma of the cervix, Dr. Newell reported 400 cases and showed that 3 per cent of these had bladder extension, and of these, 50 per cent died a renal death. So whether the tumor is primarily vesical or secondary to extension, the kidney is likely to suffer a tremendous interference. That being the case, we are obligated to protect the kidney as far as we can in diagnosis and in therapy. Of course, the only real way to do it is to get cases early. Unfortunately, we don't get them early. In this series of

cases, two years and eight months elapsed between the initial symptom and the special study. Fortunately, it is improving under medical education.

A tumor may invade well beyond its suspicious confines. We should watch the kidney and in our methods of therapy institute protective measures such as indwelling ureter catheter drainage while fulgurating, treating with radon seeds or what not or by some method of surgical procedure such as ureterostomy and nephrostomy. And, by the way, our dear Dr. Watson called our attention years ago to the value of preliminary double nephrostomy before operating upon certain tumors of the bladder in order to protect the kidneys. So we see the renal phase of bladder tumor is a very important one and Dr. Randall has brought up a live topic and one we need to heed.

DR. GILBERT J. THOMAS (Minneapolis, Minn.): I would like to ask Dr. Randall one question. In his experience, is the ureteral obstruction in the bladder section of the ureter, or does he feel that there is an obstruction in the ureter above this area? The location of this obstruction makes some difference in the method of treatment these patients will receive after our hearing this information today. Are we going to open into the bladder and treat the bladder malignancies as usual, being sure the ureteral opening is sufficient if the meatus is patent, or are we going to open the peritoneum and palpate and inspect the back of the bladder, and the lower ureter, expecting involvement here? Do you believe the obstruction is at the meatus in the bladder itself, or do you believe that there is metastasis or extension involving the lower ureter, extravesically? Can you tell which it is?

DR. GEORGE R. LIVERMORE (Memphis, Tenn.): In some of the cases you found absence of function on the affected side and in some of them you did not. Will you tell us whether there was any difference in the appearance of the orifice in the cases where you found it in comparison to those in which you did not?

DR. ALEXANDER RANDALL (Philadelphia, Pa.): I have had great trouble trying to find out what we should call these kidneys and the usual name around our clinic today (in order to be thoroughly fashionable) is that they are N. R. A. kidneys, there

being No Renal Activity. But if you wish to be very high-brow, you can call it Neoplastic Reflex Anuria.

Now the question simmers down to one factor. Of course, we have seen the usual condition where there is bilateral involvement and bilateral hydronephrosis. If we look at this plate, it being twenty-five minutes after injection, we would think it was another one of our N. R. A. kidneys, but here is a plate taken one hour and twenty minutes after injection and it shows a very definite delayed function of a hydronephrotic kidney on this side. So I am not talking of cases where obstruction causes a slow elimination or of conditions due to not taking late pictures.

Here are pictures of a woman who was treated for a number of years with what was thought to be an innocent papilloma about her right ureter. She disappeared from observation by volitionally keeping away, until she had a profuse hemorrhage and then came back. (Showing plate.) This is just a flat plate, for instance. There is the kidney shadow. This second one is the plate at thirty minutes, showing active function from the left kidney and the silent, non-functioning kidney on the right side. Here is a picture taken four hours later, and still no function from the right kidney.

This woman had a large mass the size of an egg in the right vaginal vault. It was fixed to the pelvis and was beyond the possibility of surgery. It was unquestionably malignant and secondary to the tumor of her bladder.

The pictures I just showed were taken the last day of January, 1934. The patient received an intensive course of x-ray treatment and we examined her the last day of April, 1934, three months later, at which time the vesical lesion had tremendously retrogressed, and the vaginal mass had decreased at least 75 per cent. She was the one patient in whom I had hoped we would see the late condition and a possible return of function. I thought here we would have the answer because she was certainly 75 per cent improved, yet three months after the previous pictures, we have exactly the same story. The kidney looks exactly as it does in the previous film, a functioning left side and no function at all from the normal looking right side. These pictures likewise have been taken as late as four hours after injection. I have not dared to catheterize any of these patients, for obvious reasons, and to date

have not had the opportunity to study this silent renal death at autopsy.

The mechanism whereby this silent renal death can occur is the interesting factor, because I cannot see it in any other light than a slow obstruction. I cannot picture a sudden obstruction happening, and it seems to me as though these kidneys have simply "lain down in the traces" as long as the opposite one is able to carry on bodily function. In those cases which we have studied where there have been bilateral ureteral involvement, as seen cystoscopically, there has been the picture that Chute depicted, with advanced bilateral hydro-ureters and advanced hydronephrosis.

DR. A. D. SPOONER (Milwaukee, Wis.): You might be interested in seeing four or five slides that remain in the box. These are photographs of the gross specimens of metastasis (showing slides).

I think if there is a clinical application in this study, it is that the malignancies, here reported, showing metastasis, bear out the contention of Braasch and Crenshaw—that growths of Grade I and II malignancies can be adequately taken care of by transurethral fulguration, and higher grades can probably best be taken care of by some transvesical method.

Due to the necessity of cutting down the abstract from twenty to ten minutes, I was unable to mention Dr. Cunningham's work and also that of Pasteau. The latter found that in 67 per cent of cases in which a known search was made, metastasis was found.

TREATMENT OF THE ATONIC BLADDER

WILLIAM F. BRAASCH, M.D.
and
GERSHOM J. THOMPSON, M.D. (by invitation)
From the Section on Urology, The Mayo Clinic, Rochester, Minnesota

The terms "atonic bladder" or "cord bladder" are generally accepted as referring to a condition of incompetence of the detrusor muscles of the bladder resulting from abnormal innervation. Although atony of the bladder is always secondary to some extravesical lesion, when it occurs as the result of disease affecting nerves supplying the bladder, it may, from a clinical standpoint, be regarded as primary. If this were granted, atony of the bladder resulting from obstruction at the vesical neck might be regarded as secondary. In some cases both obstruction and abnormal innervation are involved.

Although the function of the nerves involved in micturition and the mechanism of micturition are not exactly known, theories have gained general acceptance in which the parasympathetic or sacral nerves are regarded as contracting or emptying nerves, and the sympathetic or presacral plexus in control of the internal sphincter is regarded as a group of filling nerves. Impairment of the parasympathetic or emptying nerves will cause retention of urine.

The exact manner in which the so-called internal and external sphincters of the bladder and urethra function during micturition is still undetermined. The internal sphincter is composed of smooth muscle, and is supposed to be in a state of tonic contraction, relaxing automatically on emptying of the bladder. Only when the pressure of over-distention becomes great enough is the contracted status of the sphincteric muscle overcome. The function of the internal sphincter was first regarded as of little importance, for it was shown that its destruction, which frequently occurred in suprapubic prostatectomy, was not followed by any disturbance in micturition or in control of the bladder. It was evident that the external sphincter sufficed to prevent incontinence. However, in recent years the part played by the musculature involved in the so-called vesical neck, and generally referred to as the internal sphincter, has assumed greater importance. It is now recognized

that unless the internal sphincter, and particularly its dorsal portion, is completely relaxed, micturition is impeded and retention of urine will result. Inability on the part of the sphincter to relax has been called dysectasia. Failure of coördination of the muscles that are situated at the vesical neck, and that are involved in micturition, has also been considered to be a factor in causing retention. Such incoördination has been called achalasia. Although it is possible that such dysfunction is closely related to dysectasia, and that the two result from similar causes, yet retention of urine is occasionally observed when the internal sphincter may appear to be normal, and when there is no gross evidence of fixation.

Sphincteric dysfunction may result from a variety of causes which may be roughly grouped under the headings of mechanical and neurogenous. Mechanical fixation of the sphincter may result from cicatricial changes in the sphincteric and peri-sphincteric tissues secondary to chronic infection. This is well illustrated by the retention of urine that so frequently is observed with a so-called contracted vesical neck; often the sphincter is involved in cicatricial tissue so that it is unable to relax. Although prostatic hyperplasia may cause retention of urine as the result of obstruction in the prostatic tissues, the coincident sphincteric rigidity is probably a greater factor.

As the result of either chronic sphincteric dysfunction or mechanical obstruction, secondary atony of the detrusor muscles may develop. With marked retention of long standing, the atony may become so extensive that, although the obstruction is removed, contractile power returns only in part. Various methods have been attempted to determine the remaining degree of contractile power in the detrusor muscles, as well as the possibility of their becoming rehabilitated. Cystometric studies have been carried out by various observers, with varying degrees of success. Rose has maintained that the cystometer, if its readings are correctly interpreted, will give a valuable index to the actual and potential status of the detrusor muscles. It has been our experience that although cystometric data are often of corroborative value, they frequently fail to give the definite information desired. Another index to the potential contractile power of the detrusor muscles may be derived from injection of acetylcholine or mecholin. If the expulsive force of the bladder is definitely increased as the result of such injec-

tions, it is possible to assume that contractile power eventually will improve.

In recent years, we frequently have observed an interesting condition characterized by marked atony of the musculature of the bladder, with chronic retention of urine, in which evidence of prostatic obstruction could not be discovered on rectal examination, or by cystoscopy, and where physical examination, including examination of the nervous system, gives negative results. On introducing the catheter, marked reduction in expulsive force is evident. A cystogram may give an outline that is typical of so-called atonic bladder; that is, there is a smooth, round outline, instead of the irregularities of trabeculation usually observed with obstruction. On cysto-urethroscopy, the wall of the bladder will appear to be flabby and distended, with no trabeculation or other evidence of obstruction. Careful inspection may, however, disclose evidence of cicatricial changes, with more or less contracture or lack of elasticity of the tissues of the internal sphincter and vesical neck. In other cases there may be slight hyperplasia of the sphincteric tissues. These conditions may be easily overlooked unless carefully observed, and in some cases it is necessary to use a retrograde lens. The tissue present is usually not enough to cause actual obstruction, but it apparently interferes with the physiologic relaxation or coördination of the internal sphincter so as to cause urinary retention.

In treatment of this condition, an attempt should be made to remove the cicatricial or hyperplastic tissues at the neck of the bladder. The direct vision punch has proved to be admirably adapted to this purpose. It is frequently surprising how little tissue it is necessary to remove, often not more than a gram or two, to bring about the desired degree of relaxation. In order to restore vesical function, it will be necessary to remove every bit of abnormal tissue which can be seen in any portion of the vesical neck, so that it is smooth and on an even surface with the mucosa of the bladder.

The return of function of the musculature of the bladder is often slow, and several weeks or months may be required after operation before function is fully restored. Following operation it may be necessary to leave a retention catheter in the bladder for several days, and in some cases it is necessary to perform intermittent catheterization for several weeks. It will be seen that the intervals

of catheterization will increase, and the amount of residual urine will decrease, as the contractile power of the bladder returns. During the interval of recovery, intramuscular injection of acetylcholine has, in some cases, seemed to act as a nerve stimulant. Occasional instillation into the bladder of 1 ounce (30 c.c.) of 0.1 per cent to 0.2 per cent of an aqueous solution of gentian violet also will hasten the desire to void. In a few cases, complete relaxation of the sphincter is exceedingly difficult to accomplish. In some cases, relaxation is aided by postoperative dilatation, at regular intervals, with a Kollman dilator expanded to as much as 40 or 45 French. In an occasional case a spastic condition may persist, justifying resection of the presacral nerves in an effort to overcome the neurogenous imbalance.

In the past five years we have observed twenty-four patients with atonic bladder of this type. Function of the bladders of twenty of these was completely restored by freeing the internal sphincter of cicatricial or hyperplastic tissue, by the use of the transurethral punch. In three cases, although retention was overcome, complete normal function was not restored. In two cases, permanent normal function was established after resection of the presacral nerves. In case no abnormality of the internal sphincter can be discovered, evident failure of coördination may be remedied.

ATONIC BLADDER IN THE FEMALE

Because of differences in structure of the sphincter of the bladder in the two sexes, problems related to atony of the bladder in the female, are quite different from those related to the corresponding condition in the male. Although the sphincter has been described as consisting of external and internal fibers, still, from a functional standpoint, there is but a single sphincter. Atonic bladder in the female may result either from neurogenous or mechanical factors, or both. When innervation of the bladder is involved, the lesion may be localized either to the central nervous system or to the terminal nerves. With atony resulting from a lesion of a nerve, marked relaxation of the sphincter, and incontinence, are observed much less frequently in the female than in the male. The sphincter may be relaxed on urethroscopic examination, but sufficient contractile power remains, aided by accessory muscles, to prevent much, if any, leakage. Sympathetic neurectomy

may be indicated as long as the sphincter is continent, and some contractile power of the detrusor muscles remains. The imbalance between the sympathetic and the parasympathetic innervation, as it affects the vesical sphincter, is usually not as marked in the female as in the male; yet marked increase in expulsive force has been observed in several so-called atonic bladders following presacral neurectomy.

Mechanical factors involving the sphincter usually result from hypertrophy, cicatrization, or tumor. As a result of such obstruction, secondary atony of the musculature of the bladder may follow, from which complete recovery may be slow and is not always possible, even though obstructive factors are eliminated. Hypertrophy of the sphincter, causing retention of urine and secondary atony, is frequently observed. It may be due to nervous imbalance or to hyperplasia. Although it may not be easily recognized, as a rule evidence of sphincteric hyperplasia is visible on urethroscopic examination. When either of these factors is evident, incision into the sphincter, with forcible dilation, often will correct the condition. It has been our experience that in most of these cases it is necessary to remove several pieces of tissue, from different portions of the sphincter, before sufficient relaxation of the sphincter can be secured. The danger of secondary insufficiency, with slight incontinence, must be risked, but usually this is overcome as the sphincter recovers its tonus. Intermittent catheterization may be indicated for a variable period following sphincterotomy, in order to help restore the tonus of the vesical wall. What is accomplished is not removal of actual obstructing tissue, but correction of sphincteric dysectasia, with restoration of sphincteric relaxation.

MISCELLANEOUS TYPES OF ATONY

Atony of the wall of the bladder may result from injury to branches of the pelvic nerves, caused in the course of operations on the bladder, lower part of the ureter, or rectum. We have observed such atony occurring in two cases following ureterectomy, with extensive resection of the adjacent portion of the vesical wall. Evidence of atony was localized to the adjacent portion of the bladder, but was sufficient, in one case, to cause 150 c.c. of residual urine. Subsequent compensatory hypertrophy of the intact neuromusculature reduced this to 30 c.c. It was very evident that in

the course of the resection important parasympathetic fibers had been cut.

Atony of the bladder was frequently observed several years ago, following the Kraske type of operation for resection of the sigmoid. It was very evident that sacral nerves controlling the detrusor muscles of the bladder were sometimes destroyed in the course of the operation. In most instances the wall of the bladder recovered its contractile powers, at least in part. In other instances, the atony remained permanent. In recent years, modifications in the technic of posterior resection of the sigmoid have been made, which have largely obviated such injury to nerves. When injury occurs, intermittent catheterization or suprapubic drainage should be instituted without delay.

Amounts of residual urine, varying from 30 to 100 c.c., are occasionally observed in the presence of clinical evidence of senility, although no definite lesion can be demonstrated on examination of the nervous system. Rectal examination and cysto-urethroscopy may also fail to demonstrate any cause for the residual urine. Largely by exclusion, it would seem logical to infer that a lesion exists in the structures that innervate the bladder, related to the arteriosclerotic or senile changes existing in the central nervous system.

So-called hysterical retention of urine is often observed, although, curiously, not so often as in former years. In most cases it is apparently caused by a spastic condition of the sphincter, of functional origin, although secondary atony of the wall of the bladder may be noted in cases of long standing. Absence of the reflex pain that usually is observed with over-distention of the bladder is a curious feature, and must be explained on the basis of hysterical diminution in sensation.

In the treatment of atonic bladder, with evident imbalance of sympathetic and parasympathetic innervation, before considering presacral neurectomy, Learmonth has advised preliminary exploration of the lower vertebræ if there is any doubt as to the existence of vertebral or spinal abnormality. In some of these cases no somatic evidence of a neurogenic defect can be obtained. Among the local compressing agents are tumors, cartilaginous bands, meningocele, and bony spurs. Removal of such structures will, in favorable cases, permit restoration of vesical function. When im-

balance of innervation is marked by accentuation of the hypogastric influence, presacral resection has resulted in restoration, or marked improvement, of vesical function in a sufficient number of our cases to demonstrate its practical value. The indications laid down by Learmonth, for operation for neuromuscular imbalance, are as follows: (1) clinical data must point to reduction of function of the pelvic nerves, but sufficient function must remain to permit of some contraction; (2) the hypogastric nerves must be uninjured. In other words, it is inferred that the balance of vesical innervation is disturbed, and injured pelvic nerves are handicapped in their task by the braking action of normal hypogastric nerves. However, there must not be total paralysis in the distribution of the pelvic nerves, for after the brake is removed the residual expulsive force of the detrusor muscles must become equal to emptying the bladder. In addition, the patient must be continent and must have no impairment of the external sphincter muscle, and finally, renal function must be satisfactory.

Presacral neurectomy is, unfortunately, not applicable in the majority of cases in which there are lesions of the central nervous system, such as there are in tabes. However, when the external sphincter is intact, and some residual contractile power remains in the detrusor muscles, presacral neurectomy may be considered. The atonic condition of the bladder of many tabetic patients will improve following antisyphilitic treatment, particularly if treatment includes intermittent catheterization. The amount of residual urine, perhaps originally large, will be greatly reduced by such treatment and in some cases all residual urine will disappear. It is of interest that atony of the bladder secondary to tabes occurs much less frequently in the female. Presacral resection is rarely possible as a means of treatment of paralysis of the bladder following traumatic injury to the spine. As a rule, the contractile power of the detrusor muscles is completely lost, and, even though the sphincter is intact, much cannot be expected from overcoming the braking influence of the sympathetic nerves.

The non-surgical treatment of atonic bladder is of considerable importance. Particular emphasis should be laid on drainage. We are inclined to agree with Cabot, that in every case in which acute retention occurs after operation, or as the result of obstruction, the catheter should be employed to drain the bladder before its

normal capacity is exceeded. Early and repeated catheterization will prevent renal infection better than any other measure. Whether or not suprapubic drainage is done is of secondary importance. The main objective is to prevent over-distention of the bladder. However, with injuries to the spine resulting in paralysis of the bladder, the conditions are quite different. The atonic condition of the vesical musculature will not, as a rule, cause sufficient renal back pressure to injure the kidneys or ureters. Furthermore, congestion, and trauma to the bladder itself, as the result of retention, will not follow to the extent observed with intact vesical musculature. Overflow of the bladder usually will be established, and there is much less danger of ascending infection than would occur after catheterization. Recommendations that the bladder be allowed to overflow rather than that the catheter be used, have been previously suggested by a number of observers, including Plaggemeyer, Wesson and Cabot.

Chronic retention of urine resulting from an atonic bladder seems to have quite different results than the chronic retention seen in most cases of obstructive retention. Instead of impairment of the ureterovesical protecting mechanism, and impairment of ureteral peristalsis, together with reflux of vesical content often as far as the renal pelvis, such as frequently occurs in the presence of obstruction, the quite different picture seen in the presence of vesical atony, is slowly increasing residual urine and vesical decompensation. Apparently the ureterovesical barrier and ureteral peristalsis adjust themselves to the degree of impaired contractile power of the detrusor muscles, so that little or no ureteral reflux occurs. Only when ascending ureteritis has impaired the function of the lower part of the ureter will this result. It is surprising how often patients are observed who have had atony of the bladder of varying degrees for many years, without evidence in the urogram of reflux or of any impairment of the lower part of the ureter.

Patients frequently are observed who have insidious progressive urinary obstruction, and whose bladders are so distended that they reach the upper part of the abdomen. In one case, recently observed, the mass suggested a pancreatic cyst, but fortunately catheterization proved its nature and prevented abdominal exploration. Not only are such patients singularly free of fever and chills, which ordinarily accompany intermittent or acute prostatic obstruc-

tion, but as a general rule they give no evidence of retention of urea, are often unaware of any particular urinary difficulty, and, if a catheter has not been passed prior to their admission, the urine will be found negative on microscopy. The lack of renal injury in such an instance can be attributed to decompensation taking place in the detrusor muscles rather than in the ureterovesical mechanism. At any rate, lack of hypertrophy of the vesical wall has protected the kidneys.

SUMMARY

Atony of the bladder is never primary. It is caused either by abnormal innervation, by obstruction, or by both factors. However, for the purpose of clinical differentiation, atony resulting from disease affecting the innervation may be regarded as primary. Continuous retention of urine from any cause will produce atony of the vesical wall. In some cases it may be difficult to determine which factor is involved. With most cases of atony, obstruction, either primary or secondary, is the predominating factor.

The factors involving sphincteric dysfunction are: (1) imbalance of innervation, with predominance of the sympathetic or filling nerves; (2) rigidity or failure of adequate relaxation of the internal sphincter referred to as dysectasia; and (3) apparent failure of coördination of reflexes involved in the act of micturition centering in the vesical neck, to which the term achalasia has been given. The first condition can be favorably influenced by presacral neurectomy and the second condition usually can be remedied by thorough transurethral resection. Knowledge concerning cases in which other causes are operative is insufficient as a basis from which to determine treatment, but in one case of this type, presacral resection restored function to normal.

The abnormal tissue which interferes with function of the vesical neck may in some cases be easily overlooked. It is necessary to remove such tissues completely and to free every cicatricial contraction in order to restore sphincteric function. Sphincteric abnormality in the female presents problems quite different from those offered by corresponding conditions in the male. In most cases, judicious removal of sphincteric tissue will overcome retention, but subsequent presacral neurectomy may be necessary. Localized or partial atony may follow destruction of branches of the pelvic nerves

in the course of operation on the bladder. Various other types of atony may occur.

With acute retention such as often occurs following abdominal operation, the advisability of drainage of the bladder before it becomes overdistended should be emphasized. In contrast, with retention following extensive injury to the spine, overflow of the bladder should be permitted rather than catheterization.

It is evident that much still remains to be discovered in the mechanism of micturition and concerning the various lesions which may affect it.

BIBLIOGRAPHY

1. CABOT, HUGH: Personal communication to authors.
2. LEARMONTH, J. R., and BRAASCH, W. F.: Resection of the presacral nerve in the treatment of cord bladder. Surg., Gynec. and Obst., 51:494-499, (Oct.) 1930.
3. PLAGGEMEYER, H. W.: Final report on fractures of the spine in relation to changes in kidney and bladder function. Jour. Urol., 6:183-193, (Sept.) 1921.
4. ROSE, D. K., and DEAKIN, ROGERS: The cystometric diagnosis of central nervous system syphilis; a new appreciation of the term neurogenic bladder. Am. Jour. Syphilis, 13:371-390, (July) 1929.
5. WESSON, M. B.: Personal communication to authors.

LATE RESULTS IN PANMURAL FIBROSIS OF THE BLADDER

JOHN L. CRENSHAW, M.D.

From the Section on Urology, The Mayo Clinic, Rochester, Minnesota

Since Hunner's first description of "A Rare Type of Bladder Ulcer in Women," in 1914, this condition has received considerable attention. In view of its various characteristics, numerous names have been given the same condition, such as: "panmural fibrosis," "panmural ulcerative cystitis," "paracystitis," "elusive ulcer," "submucous ulcer," "interstitial cystitis," as well as "Hunner's ulcer" for its original describer.

Although at first panmural fibrosis was considered a rare condition, it was soon discovered that its apparent rarity was due to failure of recognition, and many cases have since been reported. The cystoscopic and pathologic findings have been described so often that it is unnecessary to repeat them here. I would call attention, however, to the fact that it is not always easy or possible, at the first cystoscopic examination, to distinguish panmural fibrosis with concurrent cystitis from chronic, pyogenic, areal cystitis; with time and treatment of the infectious lesion with irrigations, and so forth, the masking cystitis usually clears up and pyuria disappears, leaving the cystoscopic picture and persistent symptoms of panmural fibrosis. The symptomatic picture is often so typical that a diagnosis can be made from it alone; namely, marked frequency, both day and night; with gradually reducing capacity and increasing irritability; constant pain which can often be localized to one area in the bladder and is greatly increased by a distended bladder; frequent hematuria with vesical distention; the complete or nearly complete absence of pus in the urine in contrast with an extreme vesical irritability and usually negative urinary cultures. Although the condition occurs usually in women, Bumpus has called attention to its occasional occurrence in the male. Despite the fact that many patients have been studied and treated, we are still largely in the dark as to etiology, and the various types of treatment which have been, and still are, employed emphasize the persistence of the symptoms. From time to time the following types of treat-

ment have been advocated: surgical excision; topical application of silver nitrate, phenol, and so forth; fulguration; vesical irrigations; eradication of focal infection; overdistention; intravesical application of ultraviolet light; sympathectomy; transplantation of ureters, and so forth.

At the present time, at The Mayo Clinic, we usually try one type of treatment after another, with overdistention probably giving the best temporary results. Satisfactory overdistention can be carried out only with the patient under an anesthetic, and should be done only under observation through a cystoscope, so that the overdistention can be terminated immediately if tears appear in the mucous membrane. Fulguration gives miraculously rapid relief from pain, but the pain soon recurs, and following fulguration, as with excision, there is often a larger recurrence or multiple recurrences in other parts of the bladder.

The consensus has been that while an occasional cure may result from any of the many types of treatment, the percentage of permanent relief is nothing of which to be proud. On the other hand temporary improvement usually follows almost any sort of treatment, but is generally of short duration and the patient is soon back for something new.

What eventually becomes of the patients? Do they eventually become reconciled to their frequency and pain without actual improvement in their condition? Do renal complications finally appear as a result of vesical contraction? Do spontaneous actual cures occur?

REASON FOR, AND MATERIAL OF, THE STUDY

I have been asked so often by patients suffering from this disease, "What is the ultimate outcome?" that I have tried to follow up by letter our earlier patients, with the object of ascertaining the late results. Between 1914 and January, 1929, after excluding questionable cases and those in which some other urinary pathologic feature obscured the picture and those in which we knew the patients were dead, a diagnosis of panmural fibrosis of the bladder had been made in 123 cases. Of the 123 patients, five were men and 118 women. Of the women, ninety-three were married and twenty-five single. Obviously, all of the patients who were still alive at the time of conclusion of the study had gone from five

to twenty years since first being examined and treated at The Mayo Clinic.

Reports up to May 1, 1934, have been received on fifty-two patients, fifty women and two men. Throughout this paper, May 1, 1934, will be considered to be the present time, and a patient written of as being "now living" will be understood to have been living on that date. Accordingly, five patients are dead and forty-seven are living.

DATA ON THE PATIENTS WHO HAVE DIED

These data are given in Table I.

TABLE I. FIVE PATIENTS (ALL WOMEN) WHO HAVE DIED

Case	Reported cause of death	Time since registered at Clinic	Age at death, yrs.
1	Not reported	11 yrs.	52
2	Bladder trouble No renal disease	6 mos.	45
3	Gastro-enteritis	10 yrs.	69
4	Arteriosclerosis	5 yrs.	75
5	Carcinoma of rectum	7 yrs.	71

DATA ON THE PATIENTS WHO ARE ALIVE

These data will be given in the following paragraphs.

Sex and Age.—Forty-five of the forty-seven patients were females and two, males. At the time of the first symptoms, the oldest patient was sixty-one years of age, and the youngest, fourteen years; the average age 37.47 years. At the time of registering at the clinic the oldest patient was aged sixty-six years, and the youngest, twenty-two years; the average age was 44.19 years. The oldest patient, at present, is seventy-five years of age, and the youngest, twenty-nine years; the average age is 55.19 years.

Symptoms and Time.—The maximal duration of symptoms at the time of registration was thirty years, and the minimal, three months, average, 6.68 years. The maximal time from registration at the clinic to the present is twenty years, and the minimal, five years and five months.

At registration, all forty-seven patients had pain in the bladder; now, twenty have pain of various degrees. At registration there was no incontinence; now, one patient is slightly incontinent day and night, and the capacity of the bladder is 60 c.c. Hematuria is occasionally present in two cases.

Present Treatment.—Treatment of the bladder is not being taken by forty-one patients; regular treatment is being taken by four, and two are taking an occasional irrigation.

Temporary Effect of Various Types of Treatment.—The opinion that temporary improvement takes place following almost any type of treatment is verified in this series following various types of treatment given at The Mayo Clinic: Temporary improvement took place in thirty-five cases, but temporary improvement was absent in two cases. Ten patients did not mention whether or not temporary improvement occurred.

Renal Disease.—Judging from the value for blood urea or excretion of phenolsulphonphthalein, from roentgenologic examination, and from the presence of renal pain or renal symptoms, renal disease was not present at registration in any case. Now, according to reports received, in one case there is occasional pyelonephritis following transplantation of ureters into the bowel, and in one case, questionable nephritis (excretion of phenolsulphonphthalein 63 per cent). Considered in conjunction with the "causes of death" of the five patients who have died, there is nothing to warrant the assumption, in this series, that renal disease results from panmural fibrosis of the bladder.

Preceding and Associated Factors.—This series of cases verifies the findings of other observers as to the frequency with which acute infections, pyelonephritis, catheterization, labor, operations, and so forth, are cited as forerunners of panmural fibrosis. It also emphasizes the frequent concurrence, with panmural fibrosis, of skin diseases, goiter, neurosis and multiple operations. Pyuria, if present at first, usually disappeared entirely or was decreased so much that just a few cells were found, and usually no growth was obtained from culture of the urine.

Present General Health.—Health is graded 1, 2, 3, and 4. The poorest health is indicated as of grade 1; the best health, as of

grade 4. The health of twenty-nine patients was of grade 4; of twelve patients, grade 3; of four patients, grade 2; of one patient, grade 1, and one patient did not mention the present state of health. Of the four patients whose health was graded 2, the causes assigned by them were: one had ulcerative colitis and hemorrhoids; one, who was seventy-three years of age, had asthma; one had many complications not involving the urinary tract, and one had trouble with the bladder. The one patient whose health is graded 1 underwent amputation of the breast three weeks ago.

Final Results.—In trying to evaluate the final results in these cases, I have considered the individual's statement, as well as the present symptoms and findings such as frequency, vesical capacity, hematuria, pain, general health, and so forth. As a basis for grading these results they have been divided into five classes: (1) improved greatly, or cured; (2) improved considerably, that is reduced vesical capacity and so forth prevented cure, although many of the patients claimed to be perfectly well; (3) improved slightly or moderately; (4) condition stationary; (5) condition worse.

The final results have been infinitely better than I expected. Of the forty-seven patients, nineteen were improved greatly or cured; nine were improved considerably; six were improved slightly or moderately; of ten the condition was stationary, and of three the condition was worse. In other words, after from five to twenty years, thirty-four patients are cured or improved, and the condition of thirteen is stationary or worse.

Evaluation of Various Types of Treatment.—The effort to evaluate the various types of treatment is greatly handicapped by the small number of cases and the variety of treatments used in each case. The data are given in general in Table II.

The vesico-vaginal fistula mentioned in Table II was made thirteen years ago, after everything then advised had been tried. Leakage through the fistula is slight, but is enough to take the tension off the bladder and the patient is very comfortable. She will not consider having the fistula closed. Her vesical capacity is now 200 c.c.

The individual treatments received either at The Mayo Clinic or elsewhere were those listed in Tables III, IV, V and VI.

Some Comparisons.—These comparisons, of improvement or

TABLE II. VARIOUS TYPES OF TREATMENT IN RELATION TO RESULT

	Cases								
	Total	Irrigations	Topical applications	Resection	Fulguration	Focal infection removed	Overdistention	Other treatments	Pain now
Cured or greatly improved	19	15	10	8	8	5	2	1, colon vaccine. 1, treatment by home physician, type unknown. 1, took 2,000 sandalwood oil capsules	0
Considerably improved	9	7	5	2	1	3	3	1, injection quinine urea hydrochloride. 1, ureteral transplant, 1927. 1, permament vesico-vaginal fistula	2
Slightly or moderately improved	6	3	2	1	3	4	1	1, 9 ureteral dilations; 1, thyroidectomy	5
Condition stationary	10	6	1	0	4	2	4	2, Rovsing treatment. 1, mercurochrome intravenously. 1, ultraviolet light. 1, treatment of prostatitis. 1, operation, nature unknown. 1, dilation of contracted vagina	10
Condition worse	3	1	0	0	2	0	2	1, Rovsing treatment	3

TABLE III. ANALYSIS OF TREATMENT OF THE NINETEEN PATIENTS WHO WERE GREATLY IMPROVED OR CURED*

Treatment	Cases	Treatment	Cases
Resection only	2	Topical application, irrigation, and removal of foci	1
Resection and irrigation	2	Topical application, irrigation, removal of foci, and fulguration	1
Resection, topical application, irrigation, and colon vaccine	1	Topical application, irrigation, removal of foci, fulguration, and overdistention	1
Resection, topical application, irrigation, and fulguration	2	Irrigation, removal of foci, and fulguration	1
Resection, irrigation, and removal of foci	1	Fulguration, irrigation, and overdistention (also, patient took 2,000 sandalwood oil capsules at home)	1
Removal of foci and irrigations	1		
Topical application only	1		
Topical application and irrigation	1		
Topical application, irrigation, and fulguration	2		

*In 1 case treatment of unknown nature was given by the home physician.

TABLE IV. ANALYSIS OF TREATMENT OF THE NINE PATIENTS WHO WERE CONSIDERABLY IMPROVED

Treatment	Cases	Treatment	Cases
Overdistention and removal of foci	1	Resection, topical application, irrigation, and removal of foci	1
Overdistention, irrigation, and injection of quinine urea hydrochloride	1	Irrigation only	1
Overdistention, removal of foci, irrigation and topical application	1	Irrigation and topical application	1
Resection, topical application, and irrigation	1	Irrigation, topical application, and construction of permanent vesico-vaginal fistula	1
		Fulguration and ureteral transplantation (1927)*	1

*Patient had pyelonephritis.

TABLE V. ANALYSIS OF TREATMENT OF THE TEN PATIENTS WHOSE CONDITION REMAINED STATIONARY

Treatment	Cases	Treatment	Cases
Resection	0	Fulguration, overdistention, topical application, and ultraviolet light	1
Irrigation	1	Fulguration, removal of foci, irrigation, and dilation of contracted vagina	1
Irrigation and treatment of chronic prostatitis	1	Overdistention, removal of foci and unspecified operation	1
Irrigation and Rovsing treatment	2	Overdistention and irrigation	1
Fulguration and mercurochrome intravenously	1		
Fulguration and overdistention	1		

TABLE VI. ANALYSIS OF TREATMENT OF THE THREE PATIENTS* WHOSE CONDITION BECAME WORSE

Treatment	Cases
Overdistention	1
Overdistention and fulguration	1
Fulgeration, irrigation, and Rovsing treatment	1

*All patients probably received insufficient treatment.

TABLE VII. COMPARISON OF CURED, IMPROVED, UNIMPROVED GROUPS IN RELATION TO FACTORS OF AGE AND DURATION

		Improved greatly or cured	Considerably improved	Condition stationary	Condition worse
Age at onset of symptoms, years	Maximum	53	45	61	56
	Minimum	20	14	20	20
	Average	37.37	34.22	43.1	38
Duration of symptoms at time of registration, years	Maximum	30	10	10	12
	Minimum	¼	1	1	6
	Average	7.62	5.33	5.2	9.33

TABLE VIII. RESULTS IN THE FIRST ELEVEN AND IN THE LAST TEN CASES

	1913-1920, cases	1927-1928, cases
Cured or greatly improved	9	2
Considerably improved	1	1
Slightly or moderately improved	1	1
Stationary	0	4
Worse	0	2
Total	11	10
Resection	7	1

lack of it, in relation to age of onset of symptoms, and in relation to duration of symptoms at registration, are given in Table VII.

The Question of Delayed Recovery.—In reviewing this series one is struck with the frequency of the statement that after treatment at the clinic a number of years elapsed in which no treatment or very little treatment was given; at first, improvement was slight, but then the patients became entirely well. Are these spontaneous cures or late results of treatment?

A comparison of the results in the first eleven cases, 1913-1920, with those in the last ten cases, 1927-1928, also suggests possible delayed improvement, or that a longer period than five to seven years may be necessary to obtain the best results (Table VIII).

CONCLUSIONS

This series of cases is too small and the treatment too varied to allow any definite conclusions to be reached, but the following are suggested:

1. The end-results are greatly better than usually they are believed to be: improved or cured 72 per cent; greatly improved (claim to be well) or cured 59 per cent, cured 40 per cent.
2. Many of the "greatly improved" patients, who are well except for reduced vesical capacity, might be cured by overdistention after the ulcer had healed.
3. Panmural fibrosis does not predispose to renal disease or shorter expectancy of life; nor does it greatly influence general health.
4. Treatment should not be confined to one type if permanent results are not obtained, but one type after another should be tried over a prolonged period.
5. Resection probably should be done more than it is done in suitable cases.

BIBLIOGRAPHY

1. BUMPUS, H. C., JR.: Submucous ulcer of the bladder in the male. Jour. Urol., 5:249-253, (March) 1921.
2. HUNNER, G. L.: A rare type of bladder ulcer in women: report of cases. South. Surg. and Gynec. Tr., 27:247-292, (Dec. 15) 1914.
3. KRETSCHMER, H. L.: The surgical treatment of so-called elusive ulcer of the bladder. Jour. Am. Med. Assn., 76:990-995, (April 9) 1921.

INCONTINENCE OF VESICAL AND RENAL ORIGIN (RELAXED URETHRA AND A VAGINAL ECTOPIC URETER)

A CASE REPORT

MILEY B. WESSON, M.D.
San Francisco, California

The pathologic leakage of urine from a bladder is properly described as incontinence, but the expression is commonly used to describe the flow from a ureter that opens into the urethra, vestibule or vagina. The patient with whom we are concerned had incontinence, first from a pathologic urethra, and later from an aberrant ureter that eventually opened into the vagina. She was cured by a plastic operation on the urethra and a heminephrectomy. The case report is of particular interest because, due to incomplete examinations by various urologists, so many chances were missed to make the diagnosis of a ureter opening into a partially obliterated Gärtner's duct.

REPORT OF CASE

The patient, a sixteen year old girl, was first seen on May 6, 1931, because of urinary incontinence which had been present from her earliest recollection. She voided small amounts of urine after she had been sitting with her legs crossed; vulva pads were worn routinely, but there had never been any vaginal discharge. She was a ward of the California Department of Public Welfare, had been sent to San Francisco from one of the northern towns and had made the rounds of the public clinics, being treated in each from one to two years. On March 7, 1927, one hospital, after exhausting the clinical ingenuity of the staff and all of the laboratory facilities, varying from barium enemas to guinea pig inoculations, discharged her with the diagnosis "enuresis due to faulty training." On July 9, 1929, following cystoscopy by an excellent urologist, she was reported to have "incontinence largely functional." ("No pictures were made because the budget had been exceeded.") Stretching of the urethra with a Kollman dilator to 45F followed by 1 per cent silver nitrate injections was advised. This procedure was followed until December 1930, without any appreciable effect upon the incontinence.

Her guardian again changed clinics and this time following cystoscopy and intravenous uroselectan (Fig. 1) a diagnosis of left double kidney and relaxed vesical orifice was made. I saw her in consultation

and examined her with a Young air endoscope and a McCarthy foroblique endoscope. The posterior loop of the vesical sphincter seemed to be absent, and as the instrument was withdrawn the urethra did not close. A vaginal examination showed what appeared to be a large cystocele. With the endoscope in the urethra and a finger in the

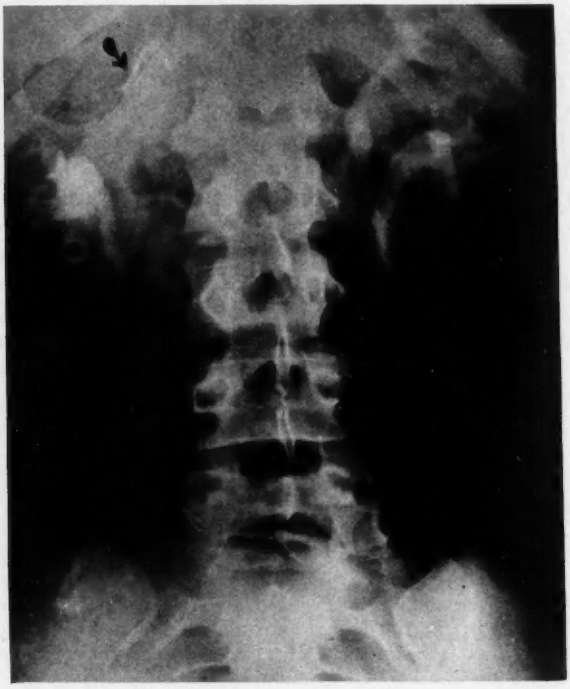


Fig. 1. Intravenous uroselectan picture which was not properly interpreted. There is a double pelvis on the left with a bifid ureter; on the right there is a single pelvis and the ureter does not show. The significance of the pelvis being at the lower pole of the kidney and a small shadow at the upper pole over the twelfth rib was not appreciated.

vagina the posterior border of the internal sphincter appeared to be exceedingly thin.

On July 10, 1931, the congenital relaxation of the vesical orifice was repaired according to Young's[48] modification of Kelly's[24] operation. A 15F Pezzer catheter was passed into the bladder. An incision was made beginning one-half inch behind the urethral orifice and extending

backwards a distance of 2 inches in the midline toward the cervix so that the neck of the bladder was in the center of the incision. The mucous membrane was about 1 cm. thick. With Mayo scissors the bladder was dissected free to a distance of 1 inch behind the head of the catheter and 1.5 inches laterally each way so that one-half of the bladder neck could be grasped between the thumb and index finger. Mattress sutures of No. 1 chromic catgut were then placed in position beginning three-fourths inch laterally to the neck of the bladder and extending forward. Four mattress sutures were used, each one being placed further laterally. The redundant mucous membrane was excised and the incision closed with continuous plain No. 1 catgut. At the end there was no bleeding from the operative site and the plicated area appeared to be at least 1 cm. in thickness. The bladder was washed with water and there was no evidence that the bladder mucosa had been penetrated by a stitch. I was called out of town that night and left the patient in the care of a urologist. Three days later, when I returned, I found that the catheter had been partially pulled out, dilating the repaired internal sphincter, and was kinked so that the overdistended bladder had leaked around the catheter. The patient passed 12 ounces at her first voiding, but there was still incontinence. Urine appeared to come from the vagina and it was assumed that this was from the urethra, but in order positively to rule out the possibility of a vesico-vaginal fistula a vaginal speculum was introduced, the bladder distended and the suture line watched. After about thirty minutes moisture appeared, but at the end of a week the suture line was tight.

Following her discharge from the hospital the patient, because of incontinence, came to my office twice a week for exercise of the vesical sphincter. She was routinely placed in the lithotomy position, with her bladder filled with mercurochrome solution. Then she was made to start and stop her stream, holding it for increasingly longer intervals. At the beginning she had very little control, but on September 30, 1931, she stated that in eight hours she had leaked only about 2 teaspoonfuls and voided normal amounts every two hours. On May 3, 1932, she gleefully reported that there was no more incontinence and she considered herself cured. A few weeks later a profuse foul vaginal discharge suddenly appeared. About an inch behind and to the right of the operative incision there was a tiny opening from which there was a sero-purulent drip. The patient was cystoscoped and catheters passed to both kidneys, a third catheter was passed through the vaginal fistula to a distance of about 1.5 inches. The bladder was filled with mercurochrome solution and indigo carmine was injected intravenously. There was no mercurochrome leakage, but indigo carmine came from all three catheters.

At a subsequent cystoscopy phenolsulphonephthalein was used and the appearance time on the right was two minutes, 40 c.c. with 20 per cent phthalein in first fifteen minutes and 10 per cent in second fifteen

minutes; on left, appearance time was two minutes, 33 c.c., 15 per cent in first fifteen minutes and 5 per cent in second fifteen minutes. From the vaginal catheters there was 50 c.c. in thirty minutes with only a trace of the dye.

A combination of intravenous neoiopax and retrograde sodium iodide

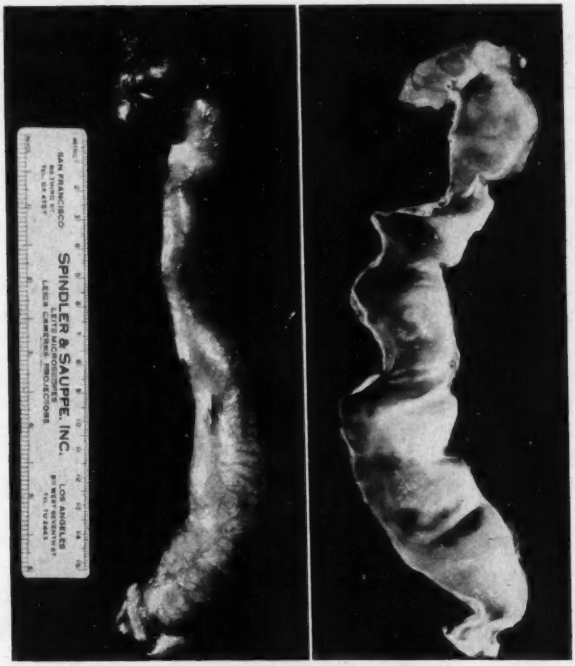
Fig. 2 *(left)*. Catheters have been passed through both ureteral orifices in the bladder and a third catheter through the vaginal opening has been injected with 13.5 per cent sodium iodide. There are two irregular sinuses leading to what appears to be a diverticulum of the ureter.

Fig. 3 *(right)*. A soft rubber catheter was passed into the bladder and a ureteral catheter into the vaginal fistula. (To hold this in place the vagina was packed with cotton.) Neoiopax was injected intravenously and 13.5 per cent sodium iodide through the catheter in the fistula.

pyelograms showed bilateral double kidneys with a bifid ureter on the left and an ectopic ureter on the right which opened into the vagina (Figs. 2 and 3).

On August 15, 1932, a right heminephrectomy and ureterectomy was done (Figs. 4*A* and *B*) with the assistance of Dr. W. G. Moore,

an eminent gynecologist. I wanted the fistulous tract traced from the vagina upward to see if it was a Gärtner's duct. However, after re-



A B

Fig. 4 *A*. Upper pole of right kidney and ureter. *B*. Ureter and kidney cut in half.

The kidney was 4 cm. by 2 cm. in area of cut surface with 1.5 cm. at one end converted into tough white fibrous tissue. The remainder is essentially normal looking. This entire mass of kidney empties into a dilated pelvis which merges into a widely dilated ureter 4 cm. across and about 25 cm. long. The wall is thin, not inflamed. Microscopically the white area is composed of small tubules reduced in number and a great excess of dense fibrous tissue between. Near the surface in the cervix there are numerous areas of round cells and attempts at tubule regeneration. There is no inflammatory reaction or evidence of infection.

moving the dilated aberrant ureter below its crossing of the normal ureter, we decided that enough surgery had been done, and the patient

had an uneventful convalescence. On October 17, 1933, she reported that she was in perfect health and was earning her own living. Now she writes that she was married in December and that her baby is expected in September, and I am very curious to try neoiopax on that infant.

The literature on ureteral ectopia has been thoroughly covered in recent years by the excellent contributions of Delmas and Delmas,[11] Mertz,[31] Harpster, Brown and Delcher,[18] Kollman,[28] Begg,[5] Herbst and Polkey,[20] Thom,[45], Sargent,[40] and Kilbane.[25] What was formerly an accidental finding at operation or autopsy is today encountered in daily clinical practice due to the employment of the newer methods of urologic examination. The condition in female patients, because of the incontinence, has usually been diagnosed during life since the aberrant ureter opened into the urethra,[29,43] the vulva[10] or the vagina and there was constant leakage in spite of normal urinary function. In males, due to the lack of incontinence, ectopic ureters were considered rare until the introduction of intravenous pyelography.

The statement has been repeatedly made that from the standpoint of development it is impossible for a ureter to open into the vagina[19] and that a study of many clinical reports shows that such openings are really in the vestibule and either the author or the translator has made a mistake in nomenclature, confusing the vagina with the vestibule.[36] To settle the question we have to turn to embryology. The vestibule is of Wolffian origin but the vagina is derived from the Müllerian duct. Although it is reasonable for a ureter to open in the vestibule, before one can leave its Wolffian attachment and open into the Müllerian system there must be a severe developmental upset.[37] The upper part of the bladder and the urachus are derived from the ventral cloaca (entoderm), while the trigone, urethra and the vestibule are in a large measure Wolffian in origin (mesoderm). In a 3.9 mm. (four weeks) embryo the primary excretory duct enters the cloaca. The following week the ureteral bud appears at 6 mm. and starts to grow laterally. At 9 mm. it has turned and is growing cranially and at 10 mm. it has reached the mesonephros, the common duct has been incorporated in the bladder and the Wolffian ducts and ureters meet at the bladder wall. In a 13 mm. (six weeks) embryo the cranio-lateral migration of the ureters has begun. At 21 mm. (seven weeks) the triangle

formed by connecting the ureteric openings with opening of Wolffian ducts (Müller's hillock) is an equilateral triangle. Throughout, the renal bud or ureter has maintained its original position but the portion of the Wolffian duct from which it regularly arose is now actually a part of the bladder—the trigone. As this process of expansion of the Wolffian duct continues, its orifice passes downward to end normally in the posterior urethra in the male as the ejaculatory ducts, and in the vestibule of the female as Gärtner's ducts. The expansion of the Wolffian duct is not uniform, the bladder trigone and the urethra being formed more at the expense of the lateral and anterior walls then of the posterior. If the renal bud is implanted low down in the duct before this descent or expansion it will open early into the bladder and accordingly be situated high up. The higher up it is in the duct the longer it will take before the part to which it is attached expands to form part of the urinary tract. It may be so high that the expansion or descent of the Wolffian duct has ceased before the part to which it is attached has opened onto the trigone in the bladder or urethra. In the male such a ureter would open into the seminal vesicle, the vas deferens, or the ejaculatory duct.[7]

In the female embryo remains of the Wolffian body are recognized as the parovarian tubules situated between the fallopian tube and the ovary.[9] They are homologous with the vasa efferentia and epididymis of the testis since they are the persistent excretory ducts of the Wolffian body.[6,15,38] All that remains of the primary excretory duct is known as Gärtner's duct. This may extend from the parovarium (epoöphoran or body of Rosenmüller) through the broad ligament. At the level of the internal os uteri the canal first sinks into the substance of the uterus and running downward through the muscle layers it gradually approaches the mucous membrane medially without reaching it, and then from the upper part of the vagina runs caudally above the middle of the lateral wall, and its opening to the exterior is immediately at or very close to the free border of the hymen through the vestibular epithelium.[32,41] This is the site of the majority of ectopic ureters in the female.[42] A ureter for obvious reasons can not open into the uterine canal or a fallopian tube[18] of a normal individual. In monsters, pathologists have found some unusual conditions.

In twin ureters there are two renal buds arising from the same

Wolffian duct (Fig. 5). If they are close together the ureteric orifices are adjacent in the bladder, the upper meatus connecting with the lower pole. But if the orifices are far apart, the lower, connecting with the superior pole of the double kidney, may not

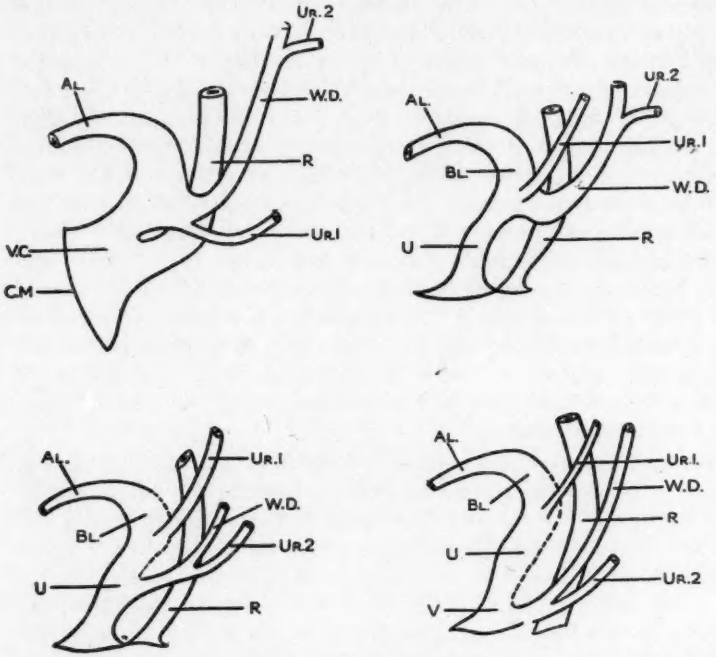


Fig. 5. Development of aberrant ureter. When there are two ureteral buds on the Wolffian duct, the distance between them determines whether both ureters shall open into the bladder, or one shall have an ectopic opening. The lower end of the duct merely expands and becomes part of the bladder wall, while that above becomes seminal vesicle and ejaculatory duct in the male, and Gärtner's duct in the female.

Ur. 1 and Ur. 2—ureteral buds; WD—Wolffian duct; R—rectum; Bl.—bladder; U—urethra; V—vestibule. (Courtesy of R. C. Begg.)

reach the urinary tract until too late to enter the bladder. Hence we know that the extravesical ureter always belongs to the upper pole. The aberrant ureter is generally dilated and has a tiny duct leading to the ureteral orifice. The superior pelvis of the kidney is usually small.

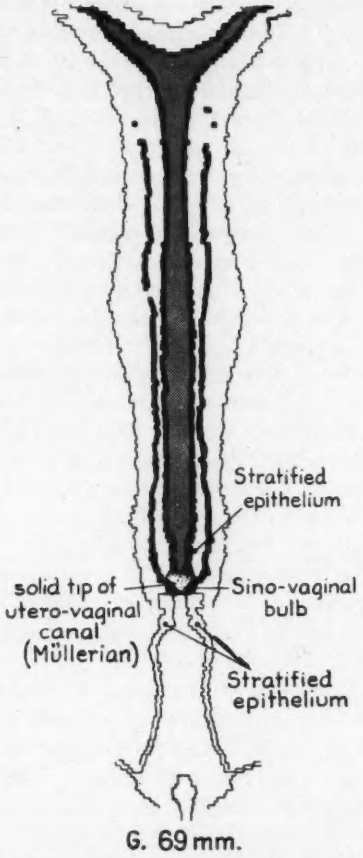


Fig. 6. Gärtner's duct (Wolffian duct) in the female extends from the parovarian in the broad ligament down to the cervix, dips superficially into it, and then passes between the urethra and vagina, and ends in the vestibule. The ejaculatory ducts in the male open on the verumontanum of Müller's hillock, while the homologue in the female ends at Müller's tubercle (sino-vaginal bulb) or the hymen. (Courtesy of A. K. Koff.)

We are inclined to question on embryologic grounds all reports of ureters opening into the vagina, but when the cystoscopist has succeeded in passing a catheter through a vaginal fistula and has made a pyelogram of the kidney, then it must be true. Emmet,[4,12] Samuels, Kern and Sachs,[39] Herbst and Polkey,[20] Sargent,[40] O'Conor,[34] Ottow,[35] Walz,[47] Kelly,[23] Katz,[22] Troup,[46] Albarran,[1] Milton,[33] and Alsberg[3] have all reported ureteral orifices in the vagina, proven by pyelography or operation, and the openings all lie in the course of Gärtner's duct. Kilbane,[25] Furniss,[14] Israel,[21] and Allenbach, Boeckel and Franck,[2] Kollman[28] and Linck[30] have reported vaginal discharges cured by a nephrectomy or the removal of the upper part of a double kidney. In Knoepfelmacher's[26] case, the diagnosis was made at autopsy. Israel's patient had a cyst in the vagina, and when this was incised a profuse vaginal discharge started which ceased following a heminephrectomy. Guibal[16] had a similar case. Allenbach, Boeckle and Franck,[2] at an exploratory operation for abdominal colic, noted a dilated ureter which they did not molest. Five days later there was a profuse vaginal discharge and the patient immediately got well. There was a return of symptoms in eight months, but the removal of the vaginal ureter and upper part of the kidney resulted in a permanent cure. Conitzer[8] reported an aberrant ureter ending in a vaginal cyst in the "upper quadrant of the vagina." Hanshalter and Jacques[17] reported a similar cyst bulging into the bladder.

Dr. George L. Streeter,[44] Carnegie Institute of Embryology, states that there is no doubt but what we were dealing with an embryologic defect of the Wolffian duct, in the case reported. There are three possibilities and had any of the urologists who treated the patient made a complete genito-urinary study, not trusting any details to others, we would know positively where the ureter originally ended.

Was this vaginal ectopic ureteral opening always present and overlooked by all of us who studied the patient during the preceding half dozen years; or did the ectopic ureter open in the dilated urethra and was cut or tied off when the plastic operation was done with resultant leakage attributed to a vesico-vaginal stitch; or did the ureter end in a partially obliterated Gärtner's duct,[27] form a cyst, abscess and rupture spontaneously? The fact that the fistula was an inch away from the healed scar of the urethral plastic and the sero-

purulent discharge did not appear until ten months after the operation is evidence that the two were not related.

Had the pyelograms been properly interpreted a more thorough search would have been made for an ectopic ureteral orifice, before doing a plastic repair upon the obvious urethral pathology present. If the upper pole secreted uroselectan, the ureter could not have a blind ending. We cured the patient's vesical incontinence but interfered with a scientific observation as to the possibility of a ureter opening into a partially obliterated Gärtner's duct, abscessing and then beginning to function actively.

490 Post Street.

REFERENCES

1. Albarran, J.: Uretère surnuméraire ouvert dans la vulva et dans le vagin. Gaz. d. Hôp., 70:743-744, 1897.
2. Allenbach, Boeckel, A., and Franck, A.: Uretère surnuméraire borgne: diagnostic pyelographique; nephro-uretèrectomie partielle. J. d' Urol. Med. et chir., Par. 21, 46-55, 1926.
3. Alsberg: Discussion, Zentralbl. f. Chir., 22:119, 1895.
4. Baker, W. H.: Malposition of the ureters. N. Y. Med. Jour., 28:575-589, 1878.
5. Begg, R. C.: Incontinence of urine of renal origin. Brit. Jour. Surg., 15:229-244, 1927.
6. Bland-Sutton, J.: Tumors, Innocent and Malignant. Funk & Wagnalls, 1911, p. 518.
7. Chwalla, R.: Entwicklung der Harnblase und der Primären Harnröhre des Menschen. Zeits. f. Gesamte Anatomie, 83:615-734, 1927.
8. Conitzer: Discussion. Zentralbl. f. Gynäk., No. 10, 266, 1895.
9. Cullen, T. S.: Vaginal cyst. Trans. Gynec. Soc., 29:459-483, 1904.
10. Davenport, F. H.: A case of incontinence of urine due to malposition of the ureter. Tr. Am. Gynec. Soc., 15:343-348, 1890.
11. Delmas, M. J., and Delmas, P.: Sur les anomalies uretèrales. Ann. d. mal. d. organes gen-urin., 28. Pt. 1, 984-1009, 1910.
12. Emmet, T. A.: Principles and Practice of Gynecology. Harry C. Lea's Son & Co., Philadelphia, 851, 1884.
13. Felix, W.: In Keibel, F., and Mall, F. P.: Human Embryology. Phila., J. B. Lippincott Co., 2:752-879, 1912.
14. Furniss, H. D.: Supernumerary ureters with extravesical openings. Jour. Urol., 8:495-505, 1922.
15. Grieg, D. M., and Herzfeld, G.: On the persistence of complete Wolffian ducts in females. Edinburgh Med. Jour., N. S., 34:701-726, 1927.
16. Guibal, P.: Un cas d' uretère surnuméraire borgne. Jour. d' Urol., 11:307-316, 1921.
17. Hanshalter, P., and Jacques, P.: Des accidents consecutifs a l'imperforation de l' extrémité vesical de l'uretère et specialment des uretères surnuméraires. La Presse Méd., Paris, 5:233-236, 1897.
18. Harpster, C. M., Brown, T. H., and Delcher, H. A.: Abnormalities of the kidney and ureter. Jour. Urol., 8:459-490, (Dec.) 1922.
19. Hepburn, T. N.: Extravesical ureteral opening causing urinary incontinence. Ann. Surg., 98:110-118, (July) 1933.
20. Herbst, R. H., and Polkey, H. J.: Ectopic ureteral openings. Jour. Urol., 17:61-72, 1927.

21. ISRAEL, I.: Diagnose und Operation einer überzahligen pyonephrotischen Niere. Berlin Klin. Woch., 55:1081-1082, 1918.
22. KATZ, H.: Beiträge zur Kenntnis der Uberzähligen Auserhalb der Blase Mundenden Harnleiter. Zentralbl. f. Gynäk.. 55:1536-1545, 1931.
23. KELLEY, S. B.: Report of a case of an ectopic ureter. Jour. Urol., 25: 241-246, 1931.
24. KELLY, H. A.: Incontinence of urine in women. Urol. and Cut. Rev., 19:291-293, (June) 1913.
25. KILPANE, E. F.: Ectopic ureteral openings. Surg., Gynec. & Obst., 42:32-49, (January) 1926; Personal communication March 10, 1934.
26. KNOEPFELMACHER. Pathological demonstration, Officelles Protokoll der K. K. Gesellschaft der Aerzte in Wien. Wien. Klin. Wchnschr., 11:297, 1902.
27. KOFF, A. K.: Development of the vagina in the human fetus. Contributions to Embryology. No. 140, Carnegie Institution of Washington, 61-91, 1930.
28. KOLLMAN, D.: Ein Fall von Pyonephrose durch Ureter-Verschlufs bei zweitteiliger Niere: ein Beitrag Zur Klinik der ueberzaehligen ureteren. Arch. f. Klin. Chir., 127:453-472, 1923.
29. KUMMELL, H., and GROFF, H.: In Garre-Küttner-Lexer; Handbuch der Praktischen Chirurgie. 5th ed., 4:385-386, 1922.
30. LINCK, A.: Pyonephrose bei verdoppelung der richten niere. Deutsche Ztschr. f. chir., 75:51-57, 1904.
31. MERTZ, H. O.: Bilateral duplication of the ureters with a compilation of recorded cases. Urol. and Cut. Rev., 24:636-642, (Dec.) 1918.
32. MEYER, R.: Zur Kenntnis des Gärtnerschen Ganges besonders in der Vagina und dem Hymen des Menschen. Arch. f. mikr. Anat., 73:751-792, 1909.
33. MILTON, H. M.: Persistent Gärtner's ducts treated in one case by diversion of opening from vagina to bladder. Lancet, 2:924, 1893.
34. O'CONOR, V. J.: Discussion. Jour. Urol., 23:376, 1930.
35. OTTOW, B.: Kritische Erwägungen zur Diagnose und Therapie der Extravesikalen harnleiterausmündung. Zentralbl. f. Gynak, 54:3239-3259, 1930.
36. PAPIN, E.: Arch. d. Mal. d. Reins. et d. Organes Gen.-urin., 1:415, 1922-23.
37. POHLMAN, A. G.: Concerning the embryology of kidney anomalies. Am. Med., 7:987-990, 1904.
38. ROUTH, A.: On cases of associated parovarian and vaginal cysts formed from a distended Gärtner's duct. Trans. Obst. Soc., Lond., 36:152, 1895.
39. SAMUELS, A., KERN, H., and SACHS, L.: Supernumerary kidney with ureter opening into vagina. Surg., Gynec. and Obst., 35:599-603, 1922.
40. SARGENT, J. C.: Ureteral ectopia. Jour. Urol., 23:357-376, (March) 1930.
41. SCHWALBE: Morphlogie der Missbildungen, Gustav Fischer 1927, 3rd teil, 12th lieferung, 3rd Abteilung, Chapters 1-3, pages 309-316.
42. SPITZER, W. M., and WALLIN, I. E.: Supernumerary ectopic ureters. Ann. Surg., 88:1053-1062, 1928.
43. STAMMLER, A.: Zur Kenntnis der aberrierenden, überzähliger Ureter. Ztsch. f. Urol. Chir., 2:241-249, 1913.
44. STREETER, GEORGE L.: Personal communication, April 27, 1934.
45. THOM, B.: Harnleiter-und Nierenverdoppelung mit besonderer Berücksichtigung der extravesikalen Harnleitermundungen. Zeits. f. Urol., 22:417-468, 1928.
46. TROUP, J.: Persistence of the complete Wolffian duct. Brit. Med. Jour., 1:707-708, 1931.
47. WALZ, W.: Zur Klinik der Enuresis Ureterica. Zentralbl. f. Gynäk., 55: 2300-2305, 1931.
48. YOUNG, E. L., JR.: Urinary incontinence in the female. Jour. Am. Med. Assn., 79:1753-1756, (Nov. 18) 1922.

DISCUSSION

DR. ALEXANDER RANDALL (Philadelphia, Pa.): I have been interested in panmural cystitis ever since Dr. Keene, Professor of Gynecology at the University of Pennsylvania, studied it about fifteen years ago. It was Dr. Allen J. Smith, Professor of Pathology, who originated the term used in the title of Dr. Crenshaw's paper. In making pathologic studies of the lesion Dr. Smith called it panmural cystitis.

I haven't at my fingers' ends our results at all, but I have come to one very definite conclusion in regard to the treatment, which is that we have obtained our best results from fulguration, but it has to be done one way. It has to be done with a fulgurating current that is so light that the electrode will not even adhere to the mucous membrane. I like to get a current with which, as I tell the assistants, I can easily paint my initials on the bladder wall, the lightest kind of fulguration. And such fulguration should be carried fully five millimeters outside the apparent area of ulceration.

SECOND DAY, MAY 15, 1934

SUPPURATING POLYCYSTIC KIDNEY

REPORT OF A CASE WITH ASSOCIATED ACUTE BILATERAL BACILLARY PYELITIS

JOSEPH F. GEISINGER, M.D.

From the Urological Service, Stuart Circle Hospital, Richmond, Virginia

Though by no means rare, polycystic disease of the kidney is yet, in the average clinic, sufficiently uncommon to command unusual attention and this becomes sharply accentuated if the given instance deviates from the ordinary clinical picture and more especially if this deviation introduces the necessity of radical surgery universally recognized to be a most unwelcome incident to this condition. Such a situation was presented by the case under review.

CASE REPORT

The patient was a young white woman, wife of a physician. Through thirty-eight years of life she had given no intimations of renal pathology and this in spite of a series of severe strains upon her system. In 1899 she passed safely through a long spell of typhoid fever. In 1918 and again in 1919 she underwent tonsillectomy. In 1921 her appendix was removed. In 1925 a contracted pelvic outlet necessitated Cesarean section for the delivery of her single child. In 1928 curettement was done for excessive menstruation and was followed by the local use of radium. About a month later, while returning from the funeral of her most intimate friend, she was struck by an automobile, receiving injury which, subsequently, required an osteoplastic craniotomy for removal of a chronic subdural hematoma. From this injury she never recovered fully. Though physically well, she became mentally so greatly disturbed that she was soon a source of incessant care and concern to her family.

Numerous urinalyses are contained in these earlier records and show nothing of any real significance. A few pus cells appear at times but mostly there is an absence of any indication of infection. On the day following craniotomy, the urine exhibited a shower of hyaline casts but there was none upon any previous or subsequent occasions. The specific gravity covered a range between 1011 and 1029. No functional dye tests are recorded but two blood urea readings were made in November, 1928, one for 28 milligrams per 100 c.c. of blood and one for 38 milligrams. At no time whatsoever was there any vesical dis-

turbance or any renal discomfort. Prior to her accident, blood pressure was low; subsequently it became elevated to 160 systolic; 100 diastolic; later it turned again toward a normal level—130 systolic, 95 diastolic, in 1932. A persistent anemia is perhaps of some significance, though this is questionable in view of a present normal blood picture. It must be admitted that these data disclose no inkling of congenital kidney disease. General history is equally insignificant in this regard, being concerned chiefly with gastro-intestinal disturbances due to absence of hydrochloric acid in the stomach; a tendency to bronchitis; menstrual difficulties, and a few minor and transient complaints. Frequent general physical examinations, including two abdominal operations, had revealed no masses.

In November, 1933, the situation underwent an abrupt change. After a trying experience in a sanitarium for her mental disorder, the patient had been allowed to return home but was being kept under careful observation. Her general physical condition seemed excellent. Her mental status, though still highly unstable, was definitely improved. Suddenly she developed pain and soreness in the left side of the abdomen and back, along with some frequency of urination and burning. Urinalysis now exhibited considerable amounts of pus and blood. X-ray for possible calculus was negative.

Upon the insistence of neurological consultants, who desired to avoid hospitalization and instrumentation if possible, a very conservative management was outlined but had to be abandoned upon the development of fever and local signs so emphatic as to suggest a possible obstructive element in the left urinary tract. Cystoscopy was performed and disclosed marked acute cystitis, congestion and edema of both orifices, pus and colon bacilli from both renal pelves. There was no significant retention in the left side, in spite of some difficulty in manipulating the catheter through the lower ureter. The status of the case, which now appeared to be one of acute bilateral pyelonephritis due to the colon bacillus, was not appreciably altered by this catheterization. Conservatism seemed indicated but rapidly demonstrated its inefficiency. The patient remained seriously ill with an occasional chill, high fever, some nausea and distention, exacerbation of an old bronchitis with distressing cough, spells of pain and soreness in the right renal area, tenderness in the left side now so marked and persistent as to compel consideration of the possibility of a surgical lesion, perhaps cortical suppuration or perinephritic involvement, though there was no historic background for either of these conditions and though it is not the habit of the demonstrated organism (colon bacillus) to participate in a clinical picture of this sort. The usual laboratory data were assembled but contributed nothing significant except normal blood urea and sharply subnormal dye excretion. Intravenous urography, though not decisive, was suggestive, and we finally reached a tentative conclusion that we were probably dealing with a tumor or with polycystic disease, attended by

infection on both sides, with complications demanding an operative procedure on one side, a situation by no means pleasant to contemplate.

The life of the patient, however, was now hanging in the balance and the necessary course, though anything but agreeable, seemed clearly marked out. Exploration of the left renal area was undertaken. The kidney was much enlarged and universally adherent to edematous surrounding tisues. Three small perinephritic abscesses were encountered containing a total of about four ounces of thick odorless pus, probably due to the rupture of infected cysts at the upper and lower poles and along the convex border. Decapsulation was then effected to relieve tension and give ready egress to any other possible surface infection. The remainder of the kidney was somewhat, but not markedly, irregular and not visibly cystic externally. Free drainage was established and the patient was returned to bed with the hope that the perinephritic situation represented the major problem and would now come under control.

This hope was not long sustained. After a temporary improvement, the patient began to go downhill again. Blood transfusion was performed without appreciable result. Temperature, previously 103 degrees, advanced two degrees. Overwhelming sepsis seemed threatening and, consequently, two days later operation was again performed. The condition of the patient was very grave and no further thought of conservatism could be entertained. The kidney was removed and proved a suppurating cystic mass throughout, cultures from which showed staphylococci and colon bacilli.

The pathologist's report on the specimen follows:

"Left kidney delivered to laboratory, measuring 15.5 cm. from upper to lower pole; 8.5 cm. from pelvis to circumference of cortex; 6 cm. anteroposteriorly. The kidney shape is preserved fairly closely, but the surface is rough and irregular. There are serrations of concave and convex areas corresponding to the underlying cysts. There are not any cysts showing thin transparent walls. The surface seems thickened and deep red in color.

"On gross section are seen, scattered throughout the kidney and immediately beneath the capsule, cysts of all sizes, the largest measuring about 2.5 by 2.5 cm. Most of the substance of the kidney is occupied by these cysts, with extremely little functional tissue left between them. Each cyst seems to be separate and distinct and not any of them communicates with the pelvis of calices. The cysts are very close together. The pelvis appears to be slightly dilated in the lower portion but for the most part is narrowed and lengthened. It is infiltrated with fat. At the upper pole of the kidney is an abscess cavity 2 by 2 cm. which contains a greenish-yellow pus. There are many smaller abscess cavities or suppurating cysts. Some of the smaller cysts contain blood-clot, a few contain serous fluid, but most of them contain a thin purulent

fluid. Grossly the cysts seem to be separated only by fibrous tissue. Very few areas, if any, appear to resemble kidney parenchyma.

"Microscopic study shows cysts very close together and of all different sizes. In many there are epithelial cells and varying proportions of pus cells and erythrocytes. In the larger cysts there are masses of pus cell debris. The cysts are lined with low cubical epithelium for the most part, but a few of the smaller ones seem to be lined with flat epithelial cells. Some of these epithelial cells are piled up like papillary buds. The walls of the cysts are surrounded by a pale-staining connective tissue and in most instances this alone fills the spaces between the cysts. There is lymphocytic infiltration and hyaline degeneration in these connective tissue areas. In some areas between cysts the renal parenchyma is seen to have undergone pressure atrophy and suppurative interstitial nephritis. The tubules appear as two layers of epithelial cells. Some tubules appear as small cysts and some Malpighian corpuscles show dilatation as if in the process of forming a cyst. Some glomeruli show hyalinization. In some areas where parenchyma appeared normal the tubules show intense cloudy swelling and many pus cells are in the lumen. Polymorphonuclear cells infiltrate all of the tissue of the kidney and in many areas there are microscopic abscesses. The arteries show a perivascular inflammation of a sub-acute nature."

A stormy postoperative course ensued, with several disheartening and threatening incidents, but with eventual recovery. Mental disturbances of major grade were more or less constantly impending but slowly subsided. One month from the date of the second operation the patient left the hospital. One week later she developed pneumonia but survived this. Today she is seemingly well, both physically and mentally. The right kidney is now thoroughly quiescent. Pyuria has disappeared with the exception of a very few cells in the voided specimen. Red cells in the blood are 5,850,000 with hemoglobin of 97.5 per cent. The blood urea is normal—30 milligrams—but the urea clearance is but 35 per cent of the normal average. The functional dye output is 28 per cent, equally distributed between the two hours. The psychopathic shock of her fearful illness has had its merciful compensation in restoring her mental equilibrium, at least for the present. For the first time in years she is free of restraints and nursing oversight. Whether she has merely left one valley for the moment and is moving unaware toward another, only time can tell.

COMMENT

It is not the purpose of this report to discuss the general characteristics of polycystic disease of the kidney already well known to this membership, from which has emanated much of the more important data relating to this interesting condition. The bilaterality of the disease, with its command for the utmost conservatism con-

sistent with the safety of the patient, is well recognized. Admittedly of congenital origin, its basic etiologic background yet remains in doubt. Numerous theories finally yielded to the hypothesis of Hildebrandt, which is now in turn under sharp criticism. The contribution of McKenna before this Association a year ago is of great interest in this connection. The clinical course of the disease with its palpable masses, its insidious nephritic picture or its explosive uremic manifestations, has been frequently described. None of these signs was visible in the present case. From a practical viewpoint, much greater interest attends the surgical aspects of the disease. Throughout the literature there runs the warning against any operative procedure not absolutely forced by dramatic circumstances. Very recently some question has been raised regarding this ultra-conservative attitude and a suggestion is being advanced that in many cases lesser indications might appropriately be accepted as justification for intervention. This appears to be the conclusion of Meltzer after a compilation of American statistics, and it is clearly set forth in the important report of Braasch reviewing the unparalleled series of cases in The Mayo Clinic. Whether or not this modification of attitude will obtain generally remains to be seen. Certainly there continues to be unanimity of opinion in the presence of the mandatory indications long recognized. The case under review is presented as coming within this latter group. The coincidence of acute bacillary and coccal infection is interesting. The extent of suppuration throughout the cystic mass is perhaps somewhat unusual. In the opinion of Keyes, such suppuration, even when chronic, is the real justification for operation, and he has performed nephrectomy in one such case. Finally, the delusive character of the ordinary urea-retention tests, pointed out by Braasch, is again evident here and is important in relation not only to this condition but to many others as well. The parallelism between the functional dye output and the urea clearance percentage, revealing deficiencies not in any way intimated by blood urea readings, suggests greater reliance upon these more sensitive indices of renal functional reserve.

TUMORS OF THE ADRENAL GLAND

A CLINICAL REPORT OF TWO CASES

HARRY CULVER, M.D.
and
MARSHALL DAVISON, M.D. (by invitation)
Chicago, Illinois

In a consideration of neoplasms of the adrenal gland attention must be directed primarily to its anatomic structure. Comparative and embryologic studies indicate that this gland consists of two separate and distinct organs, intimately united as cortex and medulla, each possessing a different origin and function. The cortex is of mesothelial origin arising from the Wolffian ridge, in common with the ovary and testes; the medulla arising from the ganglionic germ layer of the sympathetic nervous system. Clinical evidence would indicate that the cortex is intimately associated with development and growth particularly of the sex organs, while the experimental work of Cannon, together with clinical evidence, quite conclusively demonstrates the importance of the medulla in the production of epinephrin and has shown the relationship of this substance to the regulation of blood pressure and to other physiologic processes of normal life. The adrenal gland as a whole acts as a detoxifying structure, has to do with the metabolism of cholesterin and acts in close relationship with other ductless glands.

This association has been favored with two excellent papers on this subject during the last ten years, the first by Crosbie and Smith[1] in 1927 and the second by Quinby[3] in 1933. Inasmuch as little remains to be added after a careful perusal of these contributions we shall confine our remarks, for the purposes of review, to a consideration of the classification of these tumors and to the clinical aspects of two patients suffering from these growths, both of whom have made, at least temporarily, successful postoperative recoveries.

The adrenal cortex consists of three poorly differentiated layers or groups of cells, epithelial in type. Benign tumors of this structure are chiefly diffuse differentiated hyperplasias and nodular hyperplasias variously named, "strumæ suprarenales," adenomas and by Birsh-Hirschfeld hypernephromas. They have the gross and microscopic appearance of adrenal cortex with marked fat infiltra-

tion. They are very small and relatively frequent. Hypernephromas of the medulla may have their origin in misplaced cortical rests so frequently found in the medulla.

Malignant hypernephroma according to Kaufmann[2] is neither carcinoma nor sarcoma. Many pathologists, however, choose to name this type of growth as carcinoma of the adrenal gland. It shows many similarities of adrenal tissue and must be differentiated into the typical and atypical types as in the corresponding renal tumors. While the atypical type is more consistently highly malignant, there is no sharp line of demarcation in this connection. Quinby's case lends force to the probability that simple adenoma or hypernephroma may become malignant.

Cortical tumors of either benign or malignant nature frequently are associated with pecuiar sexual characteristics; the "adrenal-sexual-syndrome of Kraus," more common in females, and consists of precocity, virilism, hirsutism and secondary sex changes. The trend is toward masculine characteristics, while in males this feature may be accentuated, resulting in giant types, greatly developed genitalia associated with adult sexual physiologic phenomena.

Tumors of the adrenal medulla are of special interest. They have their analogy in other tumors of sympathetic nerves and of paraganglia. These tumors are differentiated into four groups according to the embryologic element involved—

1. Neuroblastoma arise from very immature cells, are all congenital and practically always in children under one year of age. They are very malignant.
2. Neurocytoma arise from slightly higher differentiated cells and are often clinically divided into three groups, which classification is not generally accepted:
   (a) Pepper's tumor, characterized by metastases to the liver and kidneys and usually occurring on the right side.
   (b) Hutchinson's tumor, most frequently found on the left side, with metastases chiefly to bones especially the orbit and skull.
   (c) The group in which marked anemia characterizes the picture.
3. Ganglioma arises from highly differentiated ganglion cells, are differentiated by their malignant character depending on

the grade of cell differentiation. They occur usually in females and youths and vary greatly in size.

4. Paraganglioma are chromaffin tumors consisting of fully developed chromaffin cells. They are very rare, are essentially benign and occur only in adults in distinction to other medullary tumors. They are associated with permanent or paroxysmal hypertension.

The symptomatology of adrenal tumors obviously is somewhat dependent upon the tissue involved and the time of life when their activity becomes manifest. The probability of the various developmental abnormalities becoming manifest are greater in infancy and youth than in adults after the complete development of the physical being is reached. Functional differences of histologically similar tumors can account for the different symptoms occurring in patients of the same relative age.

General symptoms of adrenal tumors are those of pressure resulting in pain, dysfunction of vital organs such as the kidney, stomach and intestines causing a variable group of symptoms due to their displacement. Fever is present in 57 per cent of the cases according to Israel.

Rowntree and Bell[4] group the cases of hypertension occurring in adrenal tumors into three main groups:

1. Those in which paroxysmal hypertension dominates the picture—usually in paraganglioma.
2. Those in which bodily configuration combined with changes in sexual characteristics are present. These indicate hyperactivity of both cortex and medulla.
3. Those in which glycosuria and hyperglycemia have constituted the prominent clinical findings and suggest a polyglandular action.

With these preliminary remarks we wish to present two clinical cases.

Case 1.—E. C., unmarried, female, aged thirty-five, entered the medical service of Cook County Hospital, September, 1933, with an examining room diagnosis of splenomegaly. She complained only of a mass in the left upper abdomen and loss of twelve pounds of weight. She had been conscious of the mass for nine months, which was definitely progressing in size. There was no discomfort of any sort. She was treated for malaria at eight years of age and had an appendectomy twelve years ago.

Menses began at fourteen years of age, regular twenty-eight day type with no variation even since the onset of her present disease.

She appeared in excellent health and nourishment to all external appearances, and physical examination revealed no abnormal findings excepting some evidence of dullness and diminished breath sounds over the lower left lung and the presence of a large firm mass in the left upper quadrant, which presented a smooth unnotched anterior border

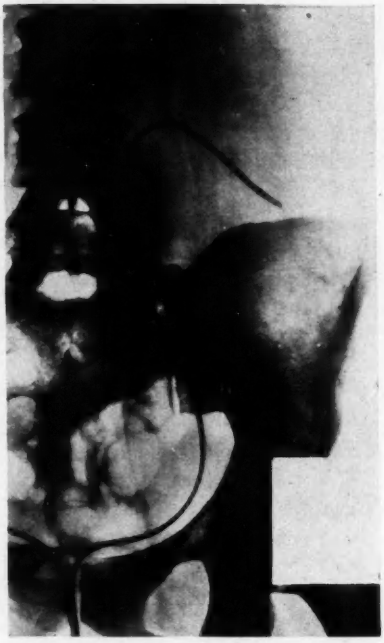


Fig. 1. Film of patient No. 1 with lead catheter in left ureter indicating the marked downward displacement of the kidney. No pyelogram available.

that extended well toward the midline and downward into the pelvis. There was a marked prominence posteriorly. The mass, while not freely movable, was not firmly fixed.

Cystoscopic examination, by the house staff, revealed a bladder normal in appearance, and normal sterile urine was obtained. The ureters were catheterized without obstruction and likewise normal sterile urine

was obtained from each kidney. The dye function of the kidneys was equal and normal. Roentgenograms revealed no unusual soft shadows but showed a markedly outward and downward course of the left ureteral catheter which ended near the iliac crest. No satisfactory pyelogram was made and the patient would not submit to re-examination.

Fig. 2. Malignant hypernephroma of the adrenal gland completely encapsulated with the removed adherent kidney, weight 3 pounds.

Visualization of the colon showed this structure displaced downward apparently by the tumor mass. The stomach likewise was normal in appearance excepting for a deformity caused by an extra-gastric mass pushing it to the right. The gall bladder showed normal visualization.

Blood examination revealed a negative Wassermann reaction, urea nitrogen of 14 milligrams per 100 cubic centimeters of blood and a blood sugar which ranged between 48 and 75 milligrams per 100 cubic centimeters of blood. The average of many blood studies revealed a hemoglobin of 75 per cent, 4,000,000 erythrocytes, and 8,000 leukocytes, while the average differential count was 64 per cent polymorphonuclears, 30 per cent lymphocytes and 6 per cent transitional cells. There were no abnormal cells noted.

The entire pre-operative course was afebrile.

From the time she was admitted to the medical ward to the time of her transfer to the general surgical service the patient was considered to have an enlarged spleen. She was transferred as a case of spleno-

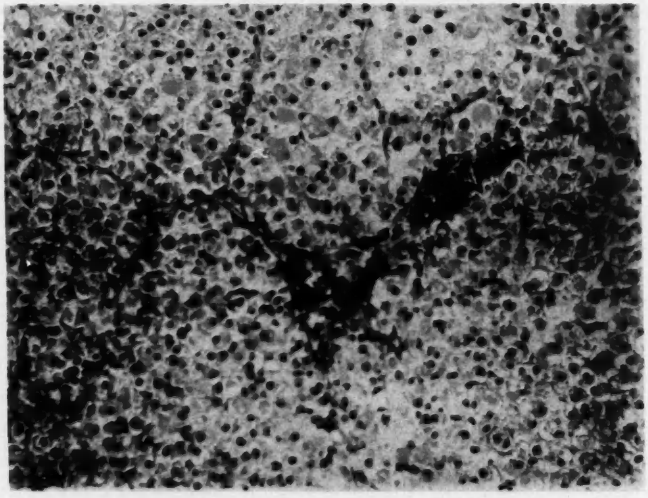


Fig. 3. Section from a representative area X 160, which shows a typical hypernephroma.

megaly of undetermined origin to one of our services (M. D.) for splenectomy.

Operation (M. D.) was performed March 2, 1934. Left diagonal upper quadrant abdominal incision revealed the spleen normal in size and displaced to the right by a large irregular extraperitoneal mass. The posterior peritoneum was adequately opened longitudinally to expose a well encapsulated, relatively soft, but not fluctuating, mass completely filling the left renal space and extending down into the pelvis. At this point it was judged to be a renal neoplasm, so the renal vessels

were isolated, ligated and cut and the mass shelled out without dangerous loss of blood. The closure was made with retroperitoneal drainage. Her blood pressure pre-operatively had averaged 132/82; six weeks postoperatively it was 120/80, a change probably not sufficient to have any bearing on the disease itself.

Surgical Specimen (Edwin Hirsch) No. 1.—This encapsulated, coarsely nodular mass, roughly the shape of a large kidney, was 25 by

Fig. 4. Left pyelogram of patient No. 2. Note inward displacement and rotation of an otherwise normal pelvis.

12 by 8 cm., and after formalin fixation weighed three pounds. The external surface was grey tissue mottled focally with yellow fatty regions and red-brown hemorrhages. On surfaces made by cutting, thin fibrous septums divided the grey tissues into compartments. The grey tissues had the consistency of a hyperplastic lymph node. The fatty regions, the hemorrhages, and the necrotic tissues varied in diameters to 5 cms. Accordingly, a considerable amount of the entire

growth had these changes. Adherent to this mass but entirely separated by a thin fibrous sheath was a kidney 10 by 4.5 by 5 cms. There were no noteworthy changes.

Histology.—Histologic preparations were stained with hematoxylin and eosin, and with phosphotungstic acid-hematoxylin. The texture of the tissues varied because of its fragile structure, edema, retrogressive changes, and incident hemorrhages. In representative places, slender vascular fibrous septums formed compartments or stalks, in or on which were mosaics of large pale-stained cells with an abundant granular cytoplasm and a fairly large compact or vesicular ovoid nucleus. The compartments formed by the septums and the septums themselves varied considerably in size. The ultimate divisions were small. The

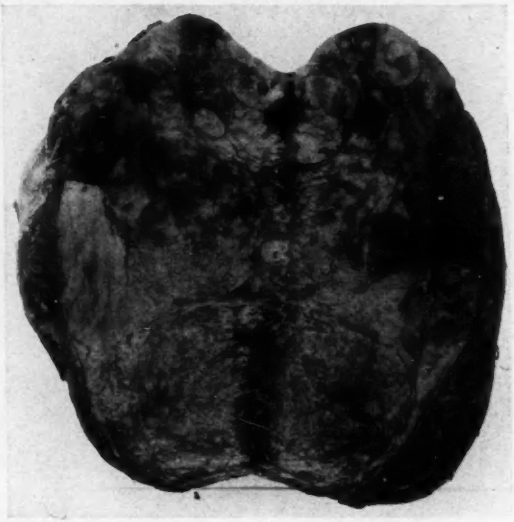


Fig. 5. Ganglioneuroma, weight 312 grams, well encapsulated, partially bisected.

tumor cell type, however, was fairly constant, although the range in the size of these cells was considerable. Only a few cells contained lipoid material staining with scarlet red and no doubly refractive substances.

Diagnosis.—Malignant hypernephroma of the suprarenal gland.

Case 2.—C. Z., female, three and one-half years of age, was admitted to the University Hospital because of an upper respiratory infection. Examination revealed a somewhat undernourished and anemic look-

ing child with a muco-purulent nasal discharge and injected, enlarged tonsils, but with clinically normal lungs. In the upper left quadrant there was a hard, irregular, seemingly painless mass appearing to rise from under the costal arch and extending downward to the level of the umbilicus. The left kidney fossa seemed to be occupied by the mass. The upper margin could not be reached under the costal arch. The lower border was uneven and rounded. There were no other abnormal findings. The blood pressure was 92/56.

Cystoscopic examination presented no difficulty and the bladder was normal to observation. Normal efflux was noted from each ureteral orifice and the left ureter was catheterized without obstruction and normal sterile urine was obtained. The bladder urine was likewise normal. Red dye given intravenously appeared from the left side in three and one-half minutes in excellent concentration.

Roentgenograms of the chest and skull were entirely negative. A film of the abdomen reveals the following findings: Adventitious calcifications are noted in the region of the spleen, which appears to be enlarged. The splenic flexure of the colon is displaced downward. The left kidney outline is not visualized. A left pyelogram demonstrates a rotated kidney lying in the midline and displaced downward. There is nothing about the shape of the pelvis and calices which would indicate a renal neoplasm. The position of the splenic flexure gas indicates that the mass is above the kidney and probably retroperitoneal.

Blood examination demonstrated a hemoglobin content of 80 per cent, erythrocytes 4,250,000, leukocytes 9,200, of which 70 per cent were polymorphonuclears, 28 per cent large mononuclears and 2 per cent eosinophiles.

Having recently had experience with Case 1, we made a pre-operative diagnosis of retroperitoneal tumor, most probably of adrenal origin.

Operation was performed March 5, 1934. An oblique kidney incision revealed a dark red retroperitoneal mass, well encapsulated and firm, in contact with, but not intimately adherent to, the kidney, which was displaced downward and toward the midline. Relatively easy blunt dissection freed the entire mass from adjacent structures. The kidney was replaced in its normal position and held there by a Deming fixation suture.

The immediate postoperative course was uneventful and the child is at this early date apparently in an excellent state of health.

Surgical Specimen (Edwin Hirsch) No. 2.—This encapsulated, smooth, elastic mass of tissue was 10 by 12 by 14 cm. and after formalin fixation weighed 312 grams. On the surfaces made by cutting the tissues were white, like the brain, only moderately firm, and were divided by septa into coarse lobular units. There were scattered hemorrhages and extensive regions of necrosis.

Histology.—Histologic preparations were stained with hematoxylin

and eosin, and with phosphotungstic acid-hematoxylin. Slender collagenous connective tissue septa formed the structural framework for the essential tumor tissues. Between these septal tissues were masses of tumor with the staining quality of brain substance but differing in the types of cells present. In the hematoxylin-eosin stained preparations, the background was granular or fibrillar and colored red.

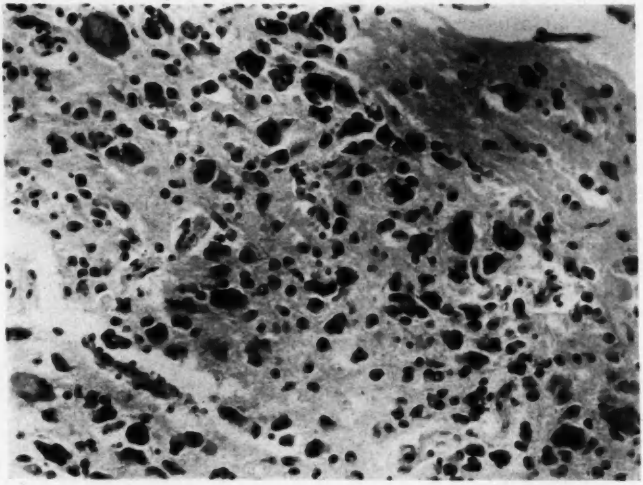


Fig. 6. Section from a representative area X 212, showing atypical ganglion cells and other less mature types as seen in glanglioneuroma.

In this were cells ranging widely in size, many small and indifferent in character; others about 15 to 20 microns in diameter with an acidophilic granular cytoplasm and vesicular nucleus; and still others larger, approaching in size ganglion cells, with one or several nuclei grouped along the periphery of the cytoplasm; and finally a few large cells (see illustration) with prolongations like a nerve fiber. The essential tumor tissues, in the sections stained with phosphotungstic acid-hematoxylin, had a background of purple staining fibrillar material comparable to that of brain tissue. Some fibrillar tissues had the general characteristics of non-medullated nerve fibers and contained elongated oval nuclei. They were continuous with the more cellular portions.

Diagnosis.—Ganglioneuroma.

Both of these patients made satisfactory immediate postoperative recoveries and are both under careful observation for signs of local or general metastases as well as evidences of adrenal insufficiency.

Since only two months have passed under this observation, obviously no conclusions can be made as to the ultimate outcome. Both surgical specimens histologically are definitely of a malignant nature, but clinicopathologic observation has demonstrated a marked variation in this characteristic of these tumors, so that time is the remaining determining factor.

Clinically these two patients are of interest to urologists chiefly in the diagnosis of upper quadrant masses; both should have been diagnosed readily, at least, as extra-peritoneal, had careful and adequate urologic study been made, but as no pyelogram was made at the time of the first cystoscopic examination of the first patient and subsequent studies were not permitted, her condition was incorrectly diagnosed as enlarged spleen on the basis of physical findings and normal differential kidney functions. A pyelogram would have shown a markedly displaced and rotated kidney with an otherwise normal pelvis which should have led to the correct location of the mass with relation to the peritoneum. Obviously this finding of kidney displacement with rotation, sometimes associated with varying degrees of hydronephrosis, is common with these tumors and should be duly considered when this finding is encountered. These findings, together with some specific clinical change known to be caused by abnormal adrenal function, simplify the problem somewhat, but where no appreciable abnormal adrenal function exists a diagnosis of extra-peritoneal tumor is all that logically could be made.

REFERENCES

1. Crosbie, A. H., and Smith, L. W.: Primary tumors of the suprarenal capsule with especial reference to adrenal virilism. Trans. Assoc. of G-U. Surg., 20:179-201, 1927.
2. Kaufmann: Pathology. Vol. II, Chapter VII.
3. Quinby, Wm. C.: Some dysfunctions caused by neoplasm, especially of the adrenal gland. Trans. Assoc. G.-U. Surg., 26:67-75, 1933.
4. Rowntree and Bell: Jour. Clin. Invest., 2:847, 1932.

PARAGANGLIOMA OF THE SUPRARENAL GLAND

CHARLES MORGAN McKENNA, M.D.,
and
LAURENCE E. HINES, M.D. (by invitation)
Chicago, Illinois

The differential diagnosis of kidney tumor and abdominal neoplasms should take into consideration tumors of the suprarenal gland. In the case to be described an abdominal mass was diagnosed tumor of the kidney because the pyelogram revealed a deformed renal pelvis and a shadow interpreted as an enlarged kidney. The removed mass revealed a large tumor of the suprarenal gland densely adherent to, but not involving, a normal sized right kidney.

CASE REPORT

Mrs. H. B., a white woman fifty-nine years old, was admitted to St. Joseph Hospital, January 26, 1934, complaining of an abdominal mass and occasional attacks of precordial palpitation. Hypertension had been discovered by a physician eighteen months before with blood pressure ranging between 190 and 160. Monthly physical examination was made after this discovery, and during one of these examinations two weeks prior to admission a mass was found in the right side of the abdomen. Other complaints were nocturia, once nightly, and constipation. She had never had any serious illnesses except twenty years ago when a fibroid tumor of the uterus was removed. No near relatives had died of any familial disease. The husband and five children were living and well.

Physical examination revealed a well nourished, youthful appearing woman not acutely ill. In the right side of the abdomen, on the approximate level with the umbilicus, there was a large, movable, smooth, slightly tender mass about as large as a small grapefruit. The mass was not connected with the liver but appeared to be arising from the right kidney region. Heart borders were within normal limits, a systolic murmur was present at the apex and the aortic second sound was accentuated. Admission blood pressure was 162 systolic and 80 diastolic; there were bilateral arcus senilis, numerous dead and crowned teeth, and slightly enlarged liver. Blood examination revealed a negative Kahn test; non-protein nitrogen was 30.0 mgs. per 100 c.c., hemoglobin 12.9 per 100 c.c.; erythrocytes 5,050,000 per cu. mm.; leukocytes 11,200 per cu. mm. The urine showed no albumin, cells or bacterial growth; intravenous phenolsulphonephthalein function test showed 5 per cent in fifteen minutes from the right kidney and 25 per cent in fifteen minutes from the left kidney. Roentgenograms after retrograde

dye had been introduced showed markedly enlarged kidney outline and a distorted, downward displaced urinary pelvis. There was an associated dilatation of the middle and inferior calices. Dr. E. L. Jenkinson, roentgenologist, intrepreted the film as evidence of a tumor or cyst of the upper pole of the right kidney. With a pre-operative diagnosis of kidney tumor a nephrectomy was performed on January 30, 1934. A very vascular, friable tumor connected to the upper pole of the right kidney and densely adherent to the surrounding connective tissue and peritoneum, was removed with considerable difficulty.

Pathologic Report of the Specimen.—A shaggy, irregular shaped tumor mass 12 by 11 by 9 cm. was densely adherent to the capsule of the superior pole of the kidney. The kidney parenchyma was not invaded by the tumor. The superior pole of the kidney was flattened and compressed to about one-half the size of the lower pole. The superior calix was smaller than the other calices. Cut surfaces of the tumor were uniformly reddish grey. Microscopic sections revealed a very cellular, vascular tumor with wide variety of cell types. In places the tumor had an alveolar type of structure and in other places there were closely packed cells with fine, loose stroma. Large syncytial cells were abundant throughout all sections of the tumor. In some portions large polyhedral cells predominated and in other portions smaller spindle shaped cells were most numerous. The large cells, when stained with chrome salts, gave a positive reaction. The pathologic diagnosis was malignant paraganglioma of the right suprarenal gland with compression of the superior pole of the right kidney.

Convalescence following the operation was prolonged due to a secondary hypochromic anemia and a persistent suppurative fistulous tract at the site of the incision. A series of deep roentgen-ray treatments were applied and the fistulous tract closed within a few days after the last x-ray treatment. A progressive fall in systolic blood pressure to 96 and a fall in diastolic to 48 occurred. At the present time the patient is in good health and shows no evidence of recurrence or metastases.

DISCUSSION

Tumors of the suprarenal gland originate either from the cortex or from the medulla. Ewing classifies suprarenal tumors as:

Cortical: (a) Hyperplasia, nodular or diffuse
(b) Adenoma
(c) Carcinoma

Medullary: (a) Focal hyperplasia of
(1) Glia tissue or
(2) Chromaffin cells
(b) Neuroma ganglionare
(c) Neurocytoma or neuroblastoma
(d) Chromatophoroma or paraganglioma

The hyperplastic cortical tumors are usually small nodular circumscribed masses. Occasionally the diffuse forms cause suprarenal enlargement as large as the kidney. Cortical adenomas are usually small single yellow tumors, ocasionally they are multiple or bilateral. Carcinomas of the cortex are often large yellow tumors adherent to the kidney and adjacent structures and subject to widespread extension and metastases.

The three types of medullary tumors of the suprarenal gland are neuroma ganglionare, neuroblastoma, and paraganglioma. The neuroma ganglionare is a rare tumor arising from the highly differentiated cells of the sympathetic nervous system of the medulla of the suprarenal gland. Although they may attain considerable size they practically never show malignant characteristics.

The neuroblastoma or neurocytoma is a highly malignant tumor which originates from the undifferentiated neuroblasts in the medulla of the suprarenal gland. Practically all of these tumors occur in infants or children, metastasize to the liver, bones and other organs and are commonly bilateral. The tumor may be yellow or grey. Histologically the typical picture of this cellular malignant tumor is a grouping of cells in clumps or rosettes. The cells usually show hyperchromatic nuclei. Occasionally one finds masses of these typical cells in the malignant forms of the paraganglioma.

The third type of tumor arising from the medulla of the suprarenal gland is the chromaffin tumor, paraganglioma, which has its origin in a neuroblast more highly differentiated than the neuroblastoma, but less mature than the neuroma ganglionare. According to Lewis and Geschickter,[2] reports of more than fifty cases of paraganglioma of the suprarenal gland have appeared in the literature. They report seven additional casees. Manasse[3] in 1893 described the first case. In a recent study by Eisenberg and Wallerstein,[1] they derive the following facts from an analysis of the reported cases: the tumors are usually benign but may be malignant; when malignant both suprarenals are involved; they occur most frequently in the fifth decade; they occur with equal frequency in both sexes; the characteristic histological features are great variability in size and shape of the cells, positive chromaffin reaction, and marked vascularity. According to these authors there is no significant relationship between this tumor and hypertension. According to Lewis et al. visceral and skeletal metastases are frequent.

COMMENT

The surgical removal of a suprarenal tumor was effected because of a diagnosis of kidney tumor. A clinical differentiation between kidney tumor and suprarenal tumor in this patient was impossible, because of the compression of the superior pole of the kidney by the mass. The mass presented the histologic characteristics of a malignant paraganglioma. The roentgenograms were misleading in this case. Hypertension prior to the operation was followed by hypotension; although this one case does not prove that the tumor had anything to do with the hypertension, the subsequent hypotension suggests some relationship. A persistent postoperative fistula was treated by deep roentgen-ray therapy and a speedy closure of the fistula followed.

REFERENCES

1. EISENBERG, A. A., and WALLERSTEIN, H.: Arch. Path., 14:818, 1932.
2. LEWIS, DEAN, and GESCHICKTER, CHARLES: Arch. Surg., 28:16, 1934.
3. MANASSE: Virchow's Arch. Path. Anat., 133:391, 1893.

DISCUSSION

DR. FRANK HINMAN (San Francisco, Calif.): The problem of diagnosis of tumors of the adrenal is extremely difficult. Most of these tumors are discovered at autopsy. There are four retroperitoneal types of tumors, namely tumors of the kidney, tumors of the adrenal, parietal tumors and unattached tumors. Usually the urologist is able to say that the tumor is retroperitoneal. But the differentiation of these four types in the retroperitoneum is sometimes impossible.

One of the most marked diagnostic characteristics, it seems to me, of a non-renal tumor is the outward displacement and rotation of the kidney pelvis, usually without any deformity or filling defect in the pelvis itself. That was very well marked in the patient of Drs. Culver and Davison except that the upper calix in this picture did show a definite filling defect.

The adrenal tumors, however, show certain clinical characteristics, as was well pointed out by Dr. Culver. The adrenal gland, as you know, is of a dual origin, the intrarenal component and the sympathetic or suprarenal component. The tumors of the intrarenal component are tumors of the cortex and they are the adenomata, the carcinomata and the melanomata, which are very rare types of tumor. The tumors of the sympathetic or suprarenal component are classified, as has been pointed out, according to their embryologic origin. The sympathogonioma occurs mostly in infants or in the fetus and has not much clinical importance. The sympathoblastoma, however, is a tumor which occurs in infants, is a very highly malignant type tumor and gives definite characteristics according to metastases. The tumor on the right side usually metastasizes to the liver and to the retroperitoneal glands. This is called the Pepper type of metastasis. Tumors on the left side metastasize by way of the cervical lymph chain to the base of the brain and to the occiput and produce exophthalmus and so forth, and such metastasis is known as the Hutchinson type. But these facts, of course, are not of much clinical importance because the growth is beyond treatment.

The ganglioneuroma is an adult tumor of sympathetic tissue ori-

gin and may occur not only in the adrenal gland but elsewhere throughout the body. The other adult type of tumor, the chromaffin tumor, pheochromocytoma, is of some clinical importance. These are rare tumors arising from the adult chromaffin tissue of the adrenal gland. Tumors of this kind that are confined to the adrenal gland probably are better called pheochromocytoma, and when they occur outside the adrenal, paraganglioma, to differentiate their location. They are characterized by paroxysmal attacks of hypertension and sympathetic instability, which occur usually periodically and are not constant.

Tumors of the cortex metastasize apparently very rapidly. We have had something like eleven cases at the University of California and only two of these patients were diagnosed before death. They show very rapid and extensive metastases to the viscera and to the glands. In these two patients that were diagnosed the definite clinical manfestations which Dr. Culver has pointed out were present. One was a boy (case of Lisser) whose parents noticed at the age of one and one-half years that he was very much overdeveloped. He had almost adult genitalia at this early age. At the age of five, he had well developed genitalia and was a boy more or less of the stature of a fourteen-year-old with well developed pubic hair and adult characteristics. He had a definite adenoma of his adrenal gland which was enucleated. It was well encapsulated, but microscopically showed very high malignancy. He apparently has been cured by the removal of this adenoma.

The other patient was a woman who showed very marked masculine characteristics. She was twenty-one years old. She also had a malignant adenoma which was removed at operation, and she is alive and well.

One thing that I particularly wish to emphasize in the diagnosis of these tumors is the fact that the kidney is displaced usually laterally and the pelvis is rotated. Of course, any tumor above the kidney in the retroperitoneal space may produce this. A chondroma arising from the eighth rib about the size of the fist, which has been seen and operated on recently, produced the same displacement of the kidney as do these tumors of the adrenal gland. I have seen two cases of unattached tumors, the so-called Wolffian cyst tumors, which were also located above the kidney and produced vary much the same displacement. So in the differential diagnosis of retro-

peritoneal tumors one is helped mostly by these various clinical syndromes which characterize the adrenal tumors.

DR. ALEXANDER RANDALL (Philadelphia, Pa.): Reporting a small group of tumors in children, particularly from the point of their proper treatment, I have included a tumor which I am convinced now was of adrenal origin, occurring in a child of six, a mass filling the whole right flank but again presenting, as Dr. Hinman has brought out, the displacement of a fairly normal pelvis. The thing was considered inoperable and was one of a small group we are reporting to illustrate the value of preoperative irradiation. With the pre-operative irradiation, this child's tumor disappeared remarkably rapidly and when she came to operation, the kidney was found to be quite normal but above the kidney was found a most peculiar, bright, lemon yellow adrenal gland. At her age, it was the simplest thing in the world to do an adrenolectomy. From the point of view of successful handling, pre-operative irradiation certainly ought to precede surgery, but not to exclude or replace ultimate operative removal.

DR. WILLIAM C. QUINBY (Boston, Mass.) The subject of adrenal tumors is an exceedingly interesting one and one in which I have no doubt whatever much progress will be made in the near future.

The matter of diagnosis is all-important, of course. In this respect I think it has not been sufficiently emphasized that a study of the sugar metabolism of individuals who are suspected of having an adrenal tumor is very important. The amount of ugar in the blood of such patients is frequently, let us say, in unstable equilibrium. One sugar estimation may not be abnormal, but if the sugar is studied over a period of possibly a week or two, I think one frequently will find irregularities of sugar metabolism. Other manifestations of these adrenal cortical tumors (not the paraganglioma; the type which causes paroxysmal hypertension) concern the skin and its appendages. You will frequently find such individuals showing hyperactivity of the oil glands, seborrhea, acne, and phenomena of that sort; and this may occur in the absence of hypertrichosis, which, to be sure, a good many of them show also.

There has been some work recently done in the direction of exploratory operations on the adrenal gland. Such operations, I

think, ought to be done more frequently than they have in the past. The successful surgical attack on these cases must come at an early period, and therefore the exploratory operation on the adrenal gland oftener than it has been employed heretofore is a justifiable procedure. We have today at our command the substance called "cortin" (or whatever other name you care to give it), the active substance of the cortex of the adrenal gland. This is of great value for it can be used as a safeguard after the removal of an adrenal gland, if the other adrenal is not for the moment sufficient; if the patient shows evidence of the condition which clinically is called Addison's disease, he can be tided over by the administration of "cortin."

All these matters are exceedingly interesting, and I am quite sure that in the future we will be seeing many more of these cases successfully treated by surgery.

DR. HARRY CULVER (Chicago, Illinois): I brought out in the text but didn't have a chance to read it just the point that Dr. Hinman brought up relative to diagnosing retroperitoneal tumors of this type, the fact that a displaced and rotated kidney probably in contact with this tumor mass meant a tumor not necessarily connected with the kidney. Also I didn't mention the fact, brought out by Dr. Quinby, in this first case, one of cortical adrenal tumor, that the blood sugar varied between 75 and 48 in successively taken estimations.

DR. CHARLES M. MCKENNA (Chicago, Ill.): I would like to say first, that the most common tumors palpable in the abdomen of children are connected with the kidney and are kidney tumors. Second, the interesting point about the case just given was that the patient never complained of any symptoms referable to the genitourinary tract. The tumor was discovered by Dr. Volini while making a general examination. The patient had no loss of weight and no frequency of urination. In other words the patient felt completely well other than having precordial pain. The pyelogram, which speaks for itself, shows the contrast fluid to be in the lower pelvis and calices of the kidney, and the upper portion is rotated. This rotation, of course, is due to the pressure of the tumor of the suprarenal gland on the upper pole of the kidney. Third, I think it is most important that the patient receive intelligent x-ray treat-

ment. I would like to emphasize the word intelligent, because so many patients receive treatment from the ordinary x-ray technicians who are nothing more than photographers. This patient on x-ray treatment has gained in weight, the fistula which was persistent after the operation is now closed, and symptomatically the patient is well.

There seems to be considerable difference of opinion with x-ray men as to when the treatment should be given. By some it is held that patients should receive the treatment before the operation, while others, as in the case just reported, administer the treatment after the operation. I think there is a lot to be learned about the value of x-ray treatment in kidney tumor.

TUMORS OF THE RENAL PELVIS

REPORT OF TWO CASES

THOMAS P. SHUPE, M.D.
Cleveland, Ohio

All reports agree that tumors of the kidney pelvis are rare in an absolute as well as a relative sense, when compared with neoplasms of the parenchyma. They occur in about 7 or 8 per cent of all tumors of the kidney and are classified into two main groups, the papillary and the solid growths. The papillary tumors comprise the benign and malignant. The sessile growths comprise the transitional cell carcinoma and the squamous cell carcinoma. To these may be added the adenoma, fibroma, and sarcoma. The origin of the latter tumors may be questionable but, clinically, they could well be included among renal pelvic tumors.

Papillary tumors are the most numerous, occurring in about 75 per cent of the cases. In a series of 337 cases collected by Swift-Joly, 120 were benign papillomata, 138 papillary carcinomata, 29 transitional cell carcinomata, and 50 were squamous cell carcinomata.

The papillomata, whether benign or malignant, are usually multiple, are quite vascular, and bleed easily. This type progresses by extension to the calices, ureter and bladder. A primary papilloma of the kidney pelvis may limit its growth to the pelvis and calices or it may show very little growth in the pelvis and multiple extensions in the ureter and bladder. The transplants show little difference in the degree of malignancy from the original tumor.

The solid tumors grow and extend by invasion of the renal vein and perirenal tissues. They metastasize remotely to the lungs, liver and bones.

The symptoms are those of any renal tumor, of hydronephrosis or of calculi. This fact, plus their rare occurrence, explains why renal pelvic tumors are seldom diagnosed before intervention. Hematuria occurs in about 90 per cent of all papillary tumors and in 50 per cent of the non-papillary growths. It is spontaneous, variable and capricious, may be small in amount for a few days and

not recur for several months. The hemorrhage may be so abundant as to cause severe anemia or retention of urine due to blood clots in the bladder. Pain is not a constant symptom although vague lumbar discomfort is quite frequent. Typical renal colic may be caused by clots in the ureter or by a tumor situated at the ureteropelvic angle. Very seldom is a tumor mass palpable and then only when there is an associated hydronephrosis or hematonephrosis. Frequency, dysuria and urgency occur when the bladder is involved by transplants which have undergone necrosis or are infected. Numerous irritating blood clots in the bladder may direct all of one's attention to that organ. Hematuria demands an immediate cystoscopy to determine the source of the blood. The bleeding may cease for several months and valuable time will be lost in making the diagnosis.

A bladder tumor is rather frequently observed and should not be allowed to obscure the true source. A small growth situated near the ureteral orifice is suggestive and demands catheterization of the ureters and pyelographic studies.

Albarran found eight bladder growths in twenty-five cases of renal pelvic tumors. Paris found five in thirty-seven. Occasionally a polyp will almost completely block the orifice of the ureter, leading to hydronephrosis and a rapid development of the growths in the pelvis and ureter. When a papilloma is seen protruding from the ureteral orifice, regardless of whether the bladder is involved, a diagnosis of renal and ureteral tumor is justified.

Urinalysis seldom gives much information although papillary debris may be obtained from a centrifuged specimen. Ureteral catheterization gives valuable information as to which side is bleeding, to the character of urine obtained and to their comparative functions. The affected kidney has an inferior function and its diminution may be extremely marked.

The greatest interest, however, in the diagnosis of renal tumors is centered on pyelography and ureterography.

In 1921 Colston and Schwartzwald called attention to the value of pyelography in the diagnosis of renal tumors. Fisher, in 1933, emphasized its importance.

Retrograde pyelography should be performed in all cases in preference to excretion pyelography. One usually is dealing with a kidney whose function is much reduced so that there is not enough

excretion of contrast material. A comparison pyelogram of the other kidney is often of value in judging the expected general contour of the pelvis. A great number of changes have been described which were caused by kidney tumors; displacement of ureter, irregular contour of pelvis, rotation, compression of pelvis, filling defects, elongation of calices and shortening of calices. Interpretation is often difficult as certain shadows could signify a renal tumor as well as a tumor of the renal pelvis. A cause of possible error exists if blood clots are present in the calices or pelvis. Pyelography should be done if possible at a time when hematuria has ceased. The deformities one sees in pyelograms must be interpreted in connection with the clinical findings, and the diagnosis of renal tuberculosis, acute pyelonephritis and renal calculi must be considered. Paris states that he is astonished that the diagnosis is so rarely made and that the usual diagnosis is hydronephrosis or renal tumor and that it is only during surgical intervention that the true condition becomes known.

PROGNOSIS

A simple papilloma due to its ability and habit of forming transplants in the ureter and bladder must be considered at all times as potentially malignant.

In the cases compiled by Mock, by Stricker and by Paris, frequency of postoperative recurrences in the ureter and bladder and the number of secondary interventions was extremely high.

The accepted operative procedure in these cases is nephrectomy and total ureterectomy. Especially is this true if the diagnosis be established due to the presence of transplants in the bladder and ureter. Israel, Beer and Hunt all insist on complete extirpation of the ureter, preferably in one stage. Hunt also removes a section of the bladder, while Colston treats the ureterovesical portion by electrocoagulation.

It is remarkable, however, that complete nephrectomy and ureterectomy have been performed so infrequently. There are several reasons which may account for the failure to do a one-stage complete extirpation in these cases, one of which may be due to failure of diagnosis and another to the fact that very often nephrectomy is quite difficult and prolonging the operation for ureterectomy would

be extremely hazardous. In the other forms of renal pelvic tumors nephrectomy is sufficient.

The papillary adenocarcinoma grows slower and metastases occur later. The squamous cell carcinoma is considered the most malignant of all tumors of the renal pelvis.

In a clinico-pathologic study of renal tumors by Quinby, a com-

Fig. 1. Case 1. Filling defect of left kidney, March 24, 1932.

parison of the pathologic findings and the clinical end-results failed to show any agreement. He concluded that there are no very significant pathologic data on which a prognosis may be based.

CASE REPORTS

Case 1.—Papilliferous adenocarcinoma. Although the origin of this tumor is in the parenchyma, its growth has been confined to the pelvis

and from a diagnostic standpoint might be considered as one of a true growth of the renal pelvis.

A man, aged forty-two, suddenly on March 22, 1932, began to pass gross blood in the urine. There were no other symptoms. The patient was first seen March 24, 1932, when the urine contained much blood.

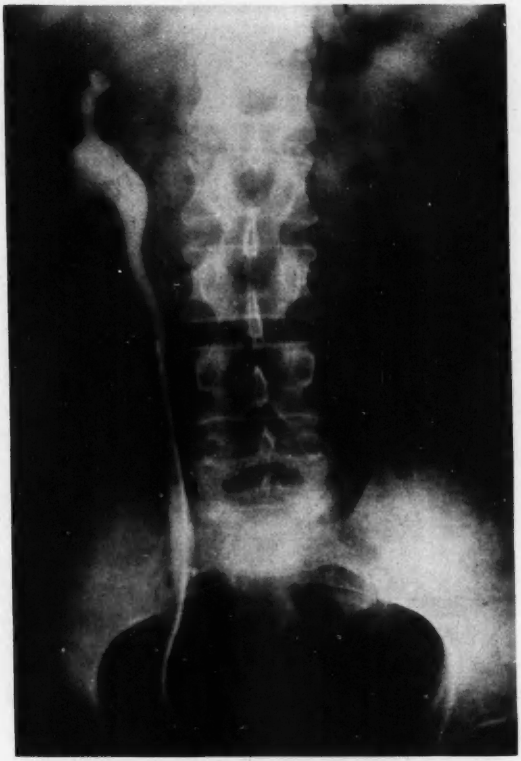


Fig. 2. Case 1. Right kidney normal, August 24, 1932.

There was a scar in the lower portion of the left chest where a rib resection had been carried out for empyema. Otherwise the physical examination was negative.

The blood pressure was 138 systolic, 80 diastolic. The white blood cell count 8,250, the red blood cell count 5,170,000, and the hemoglobin was 90 per cent. The B.U.N. was 13.74; creatinin was 2.5.

A flat kidney-ureter-bladder plate showed no evidence of any urinary calculi. The kidney outlines were well defined.

Cystoscopic examination, March 28, 1932, gave negative findings in the bladder. The urine from each kidney contained red cells. Phenolsulphonephthalein appeared from the right kidney in four minutes and

Fig. 3. Case 1. Filling defect increased in size, October 1, 1932.

from the left in five and one-half minutes. The output of dye in fifteen minutes from the right side was 18 per cent and from the left 12 per cent.

A retrograde pyelogram of the left kidney, with sodium iodide, showed no hydronephrosis. A small filling defect was present in the pelvis, the major calix was slightly increased in width and was a little

hazy. These changes suggested a lesion in the pelvis or upper pole of the kidney. A blood clot in the pelvis had to be considered, however, and no definite diagnosis was made.

The patient had no symptoms until October 1, 1932, when he again had hematuria. The hemorrhage was so profuse that retention of urine occurred due to clots in the bladder. The following day there was tenderness along the course of the left ureter and in the left flank.

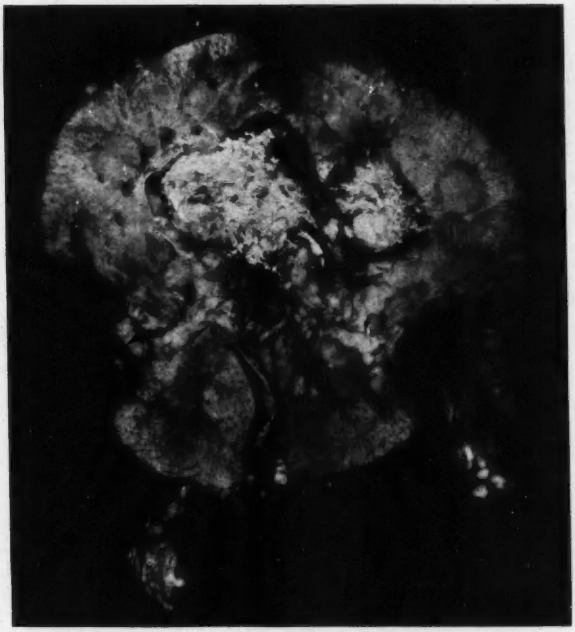


Fig. 4. Case 1. Kidney specimen. Adenocarcinoma of the renal pelvis.

Cystoscopy, October 6, 1932, showed blood from the left kidney, clear urine from the right. A pyelogram of the left kidney showed the filling defect much increased in size and a diagnosis of an intra-renal tumor was made.

Operation was performed October 24, 1932. The kidney was of an irregular shape, larger at the upper pole with a small cyst on the mesial aspect of the upper pole. The upper pole was quite adherent to the

diaphragm. The kidney and a portion of the ureter were removed. Convalescence was uneventful. The patient was discharged on the fifteenth day, the wound completely healed, and free of symptoms.

PATHOLOGIC REPORT

Gross examination.—Specimen consisted of a kidney which weighed approximately 140 grams and measured 10 by 5.5 by 4 cm. The capsule stripped with slight difficulty, leaving a smooth surface. In the upper pole of the kidney there was a cyst measuring 2 cm. in diameter. The

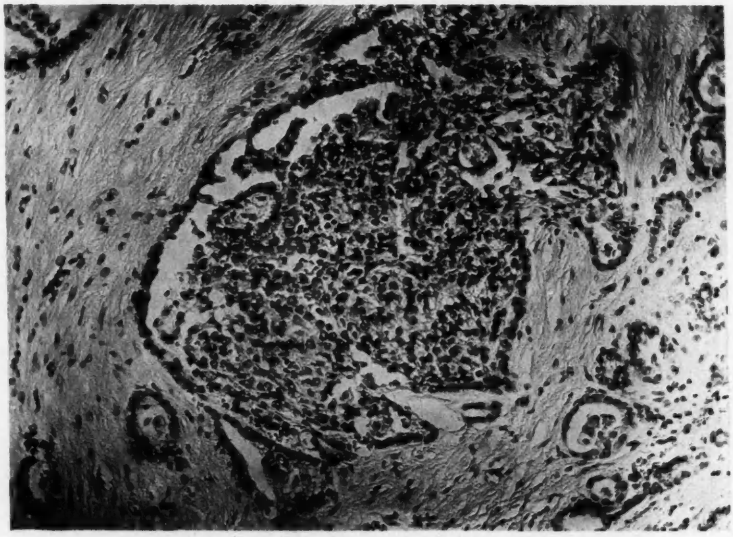


Fig. 5. Case 1. A section through the capsule of the papilliferous adenocarcinoma of the kidney. Capsular invasion with the formation of a secondary cyst and papilliferous intracystic hyperplasia is seen. The tumor is comprised of cuboidal epithelial cells which are in places disposed to form solid masses.

kidney was cut with slightly increased resistance and its surface was reddish-pink in color. The cortical striations were evident and throughout the kidney there were seen fine streaks of grayish-white tissue. Arising from the lower portion of the pelvis was a very soft, pale yellow encapsulated mass, which on section had a very fine granular appearance. It appeared to arise from the pelvis from a broad base, and completely occupied the lower pelvis. The pelvic fat was normal in amount. In the hilus the pelvis was very thin and at this point it

appeared that the tumor mass was breaking through. The tumor mass itself was very friable and appeared necrotic.

Impression.—Papilliferous carcinoma.

Histologic examination.—The section of the tumor showed it to be composed of a large mass of long, villous strands of connective tissue which were covered by tall columnar epithelium.

The epithelial covering of some of the papillæ was very irregular and the cells were pseudostratified and showed frequent mitoses.

In many of the tumor cells one could see fine granules of pigment.

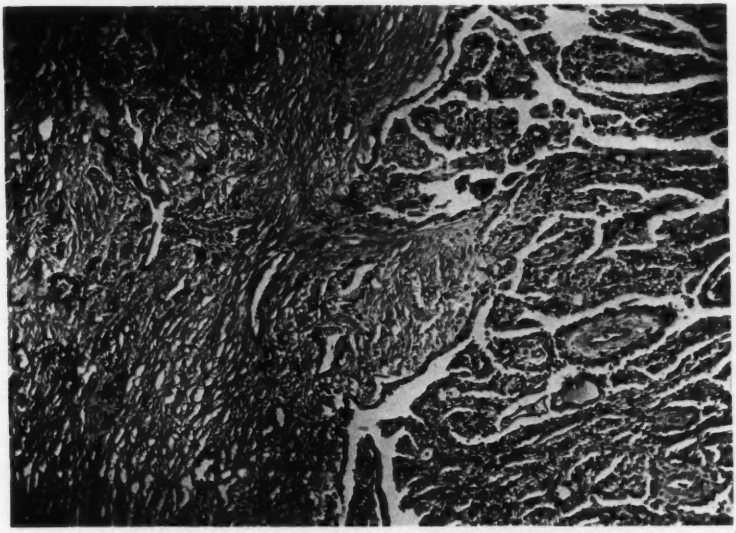


Fig. 6. Case 1. Lower magnification to show the papilliferous character of the tumor shown in Figure 5.

Throughout the tumor mass there were lymphocytes, polymorphonuclear leukocytes and eosinophiles.

Outside of the tumor mass there was a broad band of dense, fibrous connective tissue. The tumor was invading extensively. The tumor here had an adenomatous character and the gland-like structures were lined by tall columnar epithelium and there were papillary projections into the surrounding tissue.

Sections through the uninvolved kidney showed considerable fibrosis of many of the glomeruli and a few of them were completely fibrosed and the tubules in this area were atrophied.

Section through the cyst showed an area of hemorrhage with considerable cellular infiltration.

The tumor mass, although occupying almost entirely the kidney pelvis, was a well differentiated papilliferous adenocarcinoma with its probable origin in the parenchyma.

This patient has remained well since the operation and on the last examination, May 7, 1934, revealed perfectly clear urine, with no signs of any metastases.

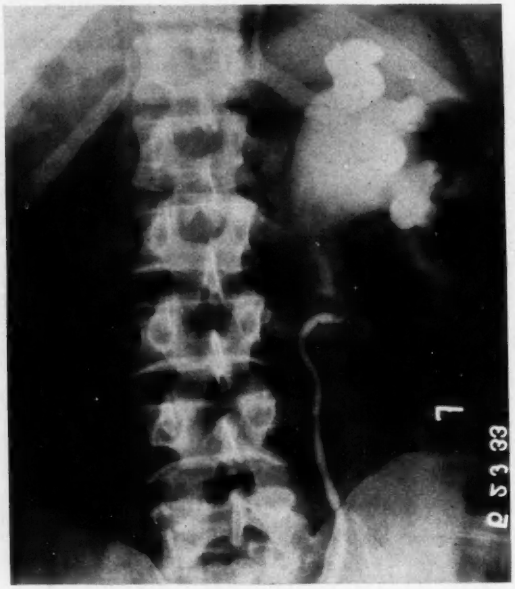


Fig. 7. Case 2. Hydronephrosis due to tumor at uretero-pelvic angle, May 23, 1933.

Case 2.—Transitional cell papilloma of the kidney pelvis.

A man, aged thirty-seven, was admitted May 22, 1933, with a history of intermittent pain in the left flank of six months' duration. There had been three such attacks previous to admission, one followed by slight hematuria, the other two showed no blood. The attacks were typical of renal colic and required morphine for relief. No calculi had been passed at any time. There was no pain or burning on urination and no symptoms of cystitis.

The physical examination showed no masses, spasms or any tender-

ness in the abdomen. The blood pressure was 130/70; the white blood count 10,200; the red blood count 5,000,000; hemoglobin 90 per cent. The B.U.N. was 38.7. Phenolsulphonephthalein tested 70 per cent in two hours. The urine on admission contained a rare white blood cell but no red blood cells or casts. The gastro-intestinal x-ray series was negative for any ulcer or tumor in the gastro-intestinal tract. A flat

Fig. 8. Case 2. Pyelogram of right kidney, normal, May 25, 1933.

kidney-ureter-bladder plate showed no shadows resembling calculi in the genito-urinary tract.

The cystoscopic examination May 23, 1933, revealed a negative bladder with a clear urine and no residual. The right and left ureters could be catheterized without difficulty. About 20 c.c. of clear urine were obtained from the left kidney, while 5 c.c. of clear urine were obtained from the right kidney. Phenolsulphonephthalein showed in five minutes from the left kidney and four minutes from the right. An output of 9 per cent of the dye was obtained from the left kidney

in twenty minutes. An injection of 17 c.c. of sodium iodide into the left ureter caused slight pain over the region of the kidney. The pyelogram showed a marked hydronephrosis of the left kidney with considerable distortion of the ureter for a distance of 5 cm. below the pelvis. There was a hazy outline of the lower third of the renal pelvis. A pyelogram of the right kidney showed nothing unusual.

Another cystoscopic examination, including a pyelogram of the left kidney, on May 25, showed essentially the same condition.

Diagnosis was made of an obstructive lesion at the lower end of the renal pelvis.

Fig. 9. Case 2. Pyelogram of left kidney, August 26, 1933.

The following day the kidney and upper portion of the ureter were exposed. A kinked ureter adjacent to the pelvis was freed of numerous adhesions. A small blood vessel extending across the ureter and running to the fascia, posterior to the kidney, was divided. This vessel acted as a sling which kept the ureter supported at a point 4 cm. below the ureteropelvic angle. After these procedures the ureter lay straight and free. The pelvis of the kidney was extensively dilated and was extrarenal. A small foreign body could be palpated in the lower portion of the dilated pelvis. Supposing this to be a stone which cast no shadow in the x-ray, the pelvis was opened; a small,

firm papillomatous tumor 1x1.5 cm. protruded from the opening. This tumor was attached to the pelvis in its lower portion by a very small pedicle not more than 2 mm. in diameter. This tumor, with a good section of the pelvis, was immediately removed and taken out of the field of operation. The opening in the pelvis was enlarged and the interior of the kidney explored. This exploration could be carried

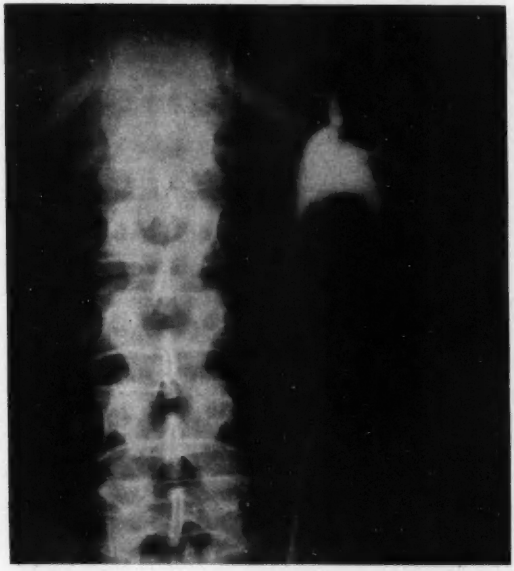


Fig. 10. Case 2. Pyelogram of left kidney, April 11, 1934.

out quite thoroughly both visually and by palpation. No other papillomatous tissue was found. A plastic procedure on the kidney pelvis was carried out and the line of incision in the pelvis closed with interrupted sutures of fine plain catgut. The wound of the muscles was closed with drainage. The convalescence was stormy but on the nineteenth postoperative day all drainage had ceased and the patient was discharged from the hospital free of symptoms.

That an extremely hazardous surgical procedure was undertaken in this case there is no doubt; therefore a careful and frequent examination has been made of this patient's kidneys and bladder. Up to April 11, 1934, he has remained symptom-free and his general physical con-

dition has improved to a point where he considers himself normal as far as endurance and well being are concerned.

A pyelogram was made of the left kidney of this patient on August 26, 1933; January 8, 1934; March 3, 1934, and the last time April 11, 1934. Urine has remained clear. There have been no attacks of pain and the pyelographic shadows show a much reduced pelvis and kidney with no filling defects.

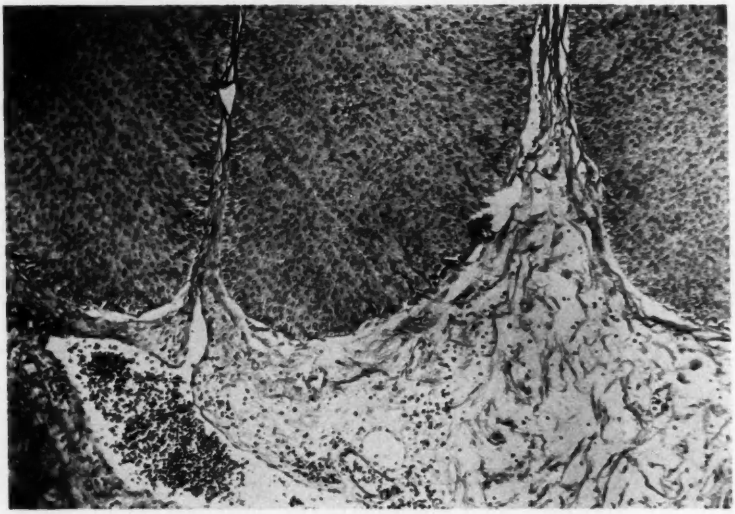


Fig. 11. Case 2. Photomicrograph of base of tumor of pelvis of kidney. There is very little evidence of invasive growth as far as that portion of the tumor submitted to the pathologist for examination is concerned.

Constant supervision of this patient for the next six years is indicated. Any signs or symptoms of a recurrence of this tumor will demand nephrectomy and ureterectomy.

PATHOLOGIC REPORT

Gross Examination.—Specimen consisted of a portion of grayish white unidentifiable tissue and an ovoid mass of pinkish-gray finely lobulated tissue which measured 1.5 cm. in its greatest axis. The tissue was cut with slight resistance, the cut surface revealing numerous, narrow, leaf-like projections radiating from a more firm grayish-white central tissue.

Impression.—Papilloma.

Histologic Examination.—The tumor consisted of papilliferous masses of uniform transitional epithelial cells supported on a delicate fibrous stroma. The epithelial cells were remarkably regular and only rarely were mitoses encountered. There was no definite evidence of stromal invasion nor invasion of renal tissue identified.

Diagnosis.—Transitional cell papilloma. Although no definite evidence of malignancy was revealed in the sections the possibility of a

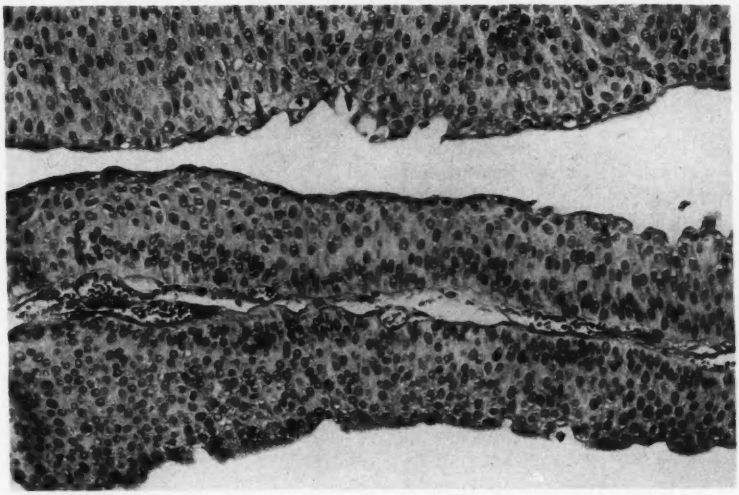


Fig. 12. Case 2. Higher magnification of transitional cell papilloma shown in Figure 11. The photomicrograph shows the uniformity of tumor cells and nuclei and the papilliferous character of the tumor.

malignant papilloma cannot be excluded. According to Broders' classification, this tumor is graded I by Dr. Karsner and Dr. Moritz.

REFERENCES

COLSTON, J. A. C.: The value of pyelography in the diagnosis of neoplasms of the kidney. Jour. Urol., 5:67-87, 1921.

FISCHER, KARL: Über Neubildungen der Niere und des Nierenbeckens. Ztschr. f. urol. Chir., 37:16-26, 1933.

FOULDS, GORDON S., SCHOLL, A. J., and BRAASCH, W. F.: A study of the histology and mortality in renal tumors. Surg. Clin. N. Amer., 4:407-424, 1924.

GERLACH, K.: Papilläre Nierenbeckengeschwulst und Narbenmetastasen. Deutsch. Ztschr. f. Chir., 239:750-757, 1933.

GRAVES, ROGER C., and TEMPLETON, EARL R.: Mixed tumors of the kidney. Jour. Urol., 5:No. 6, (June) 1921.

GROHÉ, B.: Unsere Nierentumoren in therapeutischer, klinischer und pathologisch-anatomischer Beleuchtung. Deutsche Ztschr. f. Chir., 60:1-63, 1901.

HUNT, V. C.: Papillary epithelioma of the renal pelvis. Jour. Urol., 18:225-246, 1927.

HUNT, V. C.: Method of metastasis of papillary epithelioma of renal pelvis. Surg. Clin. N. Amer., 9:853-861, 1929.

HUNT, V. C., and HAGER, B. H.: Review of 271 cases of malignant renal neoplasms. Surg. Clin. N. Amer., 9:149-159, 1929.

KIMBALL, FRANCIS N., and FERRIS, HENRY W.: Papillomatous tumor of the renal pelvis associated with similar tumors of the ureter and bladder; review of literature and report of two cases. Jour. Urol., 31:257-304, (March) 1934.

MACKENZIE, DAVID W. and RATNER, MAX: Tumors of the renal pelvis; a review of the literature and report of a case. Jour. Urol., 28:405, 1932.

PARIS, PIERRE: Les polypes du bassinet; évolution et traitement. Jour. d'Urol., 29:5-24 and 131-156, 1930.

PASCUAL, S., VAN DEN BRANDEN, F., and SWIFT-JOLY, J.: Tumours of renal pelvis and ureter. Brit. Jour. Urol., 5:323-339, 1933. (Symposium at Fifth Triennial Congress of the International Society of Urology, London, July 11-15, 1933. Discussion by Beer, Fullerton, et al.)

SCHOLL, A. J.: Papillary tumor of the renal pelvis. Surg., Gynec. and Obst., 38:186-199, 1924.

SPIESS, PAUL: Die primäre epitheliale Tumoren des Nierenbeckens und des Ureters. Centralbl. f. allg. Path. u. path. Anat., 26:553-618, 1915.

STRICKER, OSKAR: Über papillomatöse Geschwülste des Nierenbeckens. Arch. f. klin. Chir., 140:663-700, 1926.

PAPILLARY CARCINOMA OF THE RENAL PELVIS WITH METASTASES IN THE URETER AND BLADDER

X-RAY RESULTS AND AUTOPSY

ROBERT C. BRYAN, M.D.
Richmond, Virginia

Mr. F. (Huntington, W. Va.), aged fifty-one years, single, railroad contractor. The diseases of childhood were negligible. His father died of old age at seventy, his mother of cancer of the breast at fifty-two years, and his only brother of angina. His personal habits were good. For many years he had complained of indigestion and was told he had an ulcer of the stomach. In 1909 he consulted specialists for this condition, and then treated himself at intervals by going on a milk diet, rest and quiet. He would get over the attacks sufficiently well to continue with his work, having no pain or inconvenience. Fifteen years ago he contracted syphilis, and was treated for it thoroughly, with varying Wassermann reactions.

On March 5, 1928, he was suddenly taken with a severe pain in the region of the left kidney, and marked hematuria. He was hurried to the hospital in Huntington, W. Va., where cystoscopic examination was made by Doctors Bobbitt and Wilkinson, who determined that he had a hemorrhage from the left kidney. Nephrectomy was done, but the condition of the patient was so serious from loss of blood and shock that the pedicle was not tied off, but clamped, and the ureter was not explored. He was returned to bed and received large quanties of intravenous fluids.

The physician who made the microscopic report of the kidney wrote me as follows:

"The tumor was three times the size of the normal kidney, not well encapsulated, rather friable, and of an irregular shape. Sections showed the structure of a papillary growth, probably arising from the kidney pelvic epithelium, with no definite mitotic figures in the cells. There were many layers of epithelial cells, with a fibrous tissue stalk. The microscopic appearance was rather that of a papilloma, but in view of the macroscopic appearance, and of the many layers of epithelial cells, I made a diagnosis of papillary carcinoma of a low degree of malignancy, arising from the epithelium of the pelvis. In view of the fact that he has improved to such a great extent, and seems to continue so well, I am beginning to wonder if it were not an unusually large papilloma of the simple type rather than a malignant one."

The patient went through a slow and satisfactory convalescence, but

developed a large hernia at the site of the operation. As soon as his strength permitted, he went under the care of an x-ray specialist, whose treatment of him is herewith given.

"Mr. F. was referred to me March 22, 1928, and between March 22 and May 3, 1928, I gave him a series of deep x-ray treatments, reaching a biological saturation May 3; 200 peak kilovolts, 0.5 millimeter copper, 2 millimeter aluminum filter, 50 cubic millimeters skin distance, the total of which was equivalent to 1200 roentgen units back and front. Eight hundred roentgen units, or 400 milliampere minutes, with my equipment is equivalent to one erythema dose. In combination with this I gave him intravenously orthophosphate colloidal lead, except that he was given only one-half the amount as suggested. I have always regretted giving him the lead for two reasons. First, I do not believe the lead did him any harm; at the same time I don't think it did him any good. Secondly, it made him so sick that it discouraged him from taking his treatments regularly and, therefore, since saturating him I was unable to keep him saturated because he did not return for the second series until February 4, 1930, finishing the series February 19, 1930. He again returned January 28, 1931, finishing February 6, 1931. I believe the benefit Mr. F. may have derived in retarding the growth was due to the x-ray and not to the lead. I also believe the growth could have been more successfully retarded had I saturated him first and pounded at intervals of every two or three months."

Mr. F. required several months to recover sufficiently from the enormous hemorrhage he had sustained and the operation to be able to return to work. By the fall of 1928 he had gradually regained his health and strength and, but for the hernia, had no pain or discomfort. He paid little attention to himself or his condition, but in the spring of 1931 he noticed a decided discoloration of his urine, and on consulting his physician he was advised to go to Baltimore for a complete examination.

There he received further x-ray treatment and it was agreed there that the hemorrhage was most likely coming from the left ureter. The notes state that "the x-ray carried out here was given through three portals—the left lumbar, the left hypogastric and the left lateral; the dosage administered was just under an erythema dose."

On June 10, 1931, Mr. F. came to Richmond and entered Stuart Circle Hospital. He was rather tall and weighed 160 pounds (usual weight 185 pounds). He looked somewhat pale, but complained of no pain or discomfort other than the constant discoloration of the urine.

Findings in examination of the head, special organs and lungs were negative. Many of his teeth had been extracted and he wore a plate. The heart sounds were distant but there were no murmurs. There was an accentuation of the second aortic. The blood pressure was 148/86.

The following serologic reports were noted: The Wassermann and

Kahn tests were negative, urea 36 mg., sugar 100 mg., red blood cells 4,000,000, hemoglobin 85 per cent, white blood cells 5,800. The urinalysis was negative but for the four plus blood.

An x-ray was made on June 18 and reported as follows: "X-ray of the chest is negative except for some enlargement of the heart. Esophagus and stomach negative. The first part of the duodenum shows a defect which we take to be due to an ulcer. Six and twenty-four hour examinations are negative. The descending colon extends out into a large hernial sac but no defects are noted in the colon."

The abdomen was slightly asymmetrical from the very large hernia in the left flank, for which he wore a firm, canvas belt. There was some tenderness on deep pressure just below the tenth costal cartilage on the right. The lower pole of the right kidney was easily palpated, and was apparently enlarged. The left inguinal, lumbar and hypogastric regions were devoid of hair, and were of a deep brown, sunburn color, the evident lead plate border of demarcation internally being limited very sharply by a vertical line parallel to the mesial plane and just along the margin of the rectus muscle. The limit inferiorly was likewise readily seen parallel with Poupart's ligament and slightly below it, and the posterior limits were less well defined, but were overlapping and abrupted about the outer margin of the lumbar muscles. The underlying tissues were firm, dense, hard and resistant, contrasting very markedly with the normal, elastic belly wall of the right side of the abdomen. The patient had noticed a constant anhidrosis in this region and experienced a slight, burning, uncomfortable sensation, so that cold cream, albolene and goose grease were used at times upon the skin.

We hesitated in the face of this evident x-ray response of a general localized subdermal fibrosis to operate, so that the patient was kept in the hospital one month (to July 9) before surgical intervention was carried out. During this interval he was treated for the duodenal ulcer and gained considerably in weight and appearance. The tenderness over the pyloric region on deep pressure entirely disappeared.

On July 2, as there was continuance of blood in the urine, a cystoscopy was made. The 24 F. cystoscope entered with difficulty due to a moderate engorgement of the prostate. The bladder mucosa was normal. The ureteral ora were located and the left os readily catheterized with a No. 5 F. leaded ureteral, flute-pointed catheter through which there was no drainage, although washing of the catheter gave a distinctly bloody tinge. A ureterogram with 12.5 per cent solution of sodium iodide was carried out, but since we did not know the caliber, capacity or length of the left ureter we were extremely cautious not to over-distend this ureter for fear of rupture, so only a few cubic centimeters were injected. The picture was not determinative.

On July 3 examination of the urine showed four plus blood. The cystoscopy was repeated and 16 cubic centimeters of 12.5 per cent

solution of sodium iodide were gravitated into the left ureter and a ureterogram taken. This picture was very satisfactory and showed the ureter going as high as the second lumbar vertebra. No metastases were seen, and there was an irregular dilatation of the ureter. The right kidney was slightly enlarged and the spine showed arthritic changes.

On July 9, 1931, the patient was prepared for operation. He was given a general anesthetic (nitrous oxide), and a left pararectus vertical incision was made down to the peritoneum, which was stripped inward and the ureter identified. It was quite large and irregular in its caliber, and of a grayish anemic color. There were many peri-ureteral adhesions, and some of the more dense were tied off although there was no bleeding. The ureter was finally dissected free from the old kidney stump above, to its insertion into the bladder and removed. Careful examination along the course of the spine, deep lumbar muscles, about the stump of the kidney and abdominal aorta showed no glands or any evidences whatever of lymphatic enlargement or metastases, although there was a very marked and evident anemia and whiteness of the tissues throughout.

Dr. Beck, pathologist to Stuart Circle Hospital, reported as follows: "Papillary carcinoma, Grade 2. The ureter is greatly enlarged and the papillary carcinoma is growing into and filling the lumen. There is no invasion of malignant cells into the serous coat of the ureter. No evidence of metastases outside of the ureter." Two small rubber wicks were put deep into the wound as far as the ureteral bed, one above and one below, and brought out at the upper angle of the wound. The tissues were approximated in layers with catgut No. 1 and equisitine supporting sutures through the skin.

It was noted at the time of the operation that the tissues were hard and indurated, and that there was practically no bleeding whatever, either from the skin or deeper structures. Probably the entire amount of blood lost could have been absorbed easily with one-fourth of a sponge.

Between July 9 and 31 there had been an apparent satisfactory healing of the wound, although the tissues about the incision for some distance in every direction were indurated, bluish, hard, pitted slightly on pressure, and were painless. The incision had apparently united beautifully except for a small opening at the upper angle corresponding to the size and shape of the retained drainage wicks which had been removed July 14, there being no escape of blood or serum.

The patient's condition was so satisfactory, temperature, pulse and respiration normal, and he was eating well, that he was allowed to go to Old Point with a nurse on July 21. On August 6 he called me over the telephone and stated that the wound had broken open pretty much throughout its entire length, was gaping, not bleeding but had a little watery drainage. He was advised to stay in bed, and throw no undue strain upon the wound.

On August 12 he was re-admitted to Stuart Circle Hospital. Examination of the wound at that time showed it to be about 3 inches long and probably 1.5 inches wide at the middle. The walls were firm and hard and shelved downward to meet each other at about the lower level of the abdominal muscles, but there was a deeper hole at the upper angle of the wound which extended backwards and downwards probably as far as the lumbar muscles. The wound was covered with a heavy, tenacious, grayish membrane, in the fibers of which could be seen yellowish clumps of adherent pus and mucus. An attempt was made to cleanse it with peroxide, but practically no change was seen in the wound after the cleansing. The margins of the wound were firm, and for some distance back the skin was dark blue, practically painless, indurated and still pitted on pressure. We did not attempt a biopsy for fear of further damage, and several surgeons agreed that it had none of the appearances of malignancy.

Serologic examinations were again taken. The Wassermann and Kahn tests were again negative; hemoglobin 80 per cent, red blood cells 4,000,000, white blood cells 7,800, sugar 99 mg. Smear from the wound showed staphylococcus and rare chain of streptococcus. The urinalysis was practically negative, with no blood. Temperature was 98.2, pulse 80.

Balsam of Peru and castor oil were used twice daily for two weeks with no beneficial or stimulating results. For the following seventeen days the wound was treated with ultraviolet rays with the following time exposures, beginning with one and one-half minutes, then two, three, three, six, six, seven, seven, eight, eight, nine, eight, eight, seven, six, six, six. During this time the wound was dressed only with boric acid solution, and an attempt was made to strap it together with adhesive, but this proved to be so irritating to the skin that it had to be removed. Beginning September 1, pepticine digestant was used for three days, but this apparently had no effect in clearing up the wound, it still having the heavy, tenacious, grayish membrane. Boric acid was again used with apparently no cleansing or stimulating effect. At no time had there ever been the slightest discoloration by blood.

One thousand maggots were put in the wound September 15 under the usual precautions of a very fine meshed copper wire retaining cage. Many of the maggots escaped around and through the cage and were destroyed outside; however, quite enough remained. The patient complained of no discomfort from the violent activity of these maggots, only the psychologic effect of their presence was distressing to him. The heavy grayish membrane was certainly being cleaned up, and the wound looked much better, but on the morning of September 18 he complained bitterly of a sharp lancinating pain about the left upper margin of the wound, which we took to be due to an exposed nerve, that we could not see but could pretty well locate by touching. With the smallest hypodermic needle, a few minims of a 1 per cent solution of novocain were injected into this area. The tissues being so in-

durated, a spray of the novocain came back into the wound causing an immediate huddling of the maggots and cessation of their violent activities. Evidently the spray of novocain had destroyed them. There remained only some ten or twelve which showed any evidences of life. The following day these, too, were removed, the wound cleansed, and a 1-7000 bichloride dressing was generously applied. This preparation was used until October 8. On October 1 heliotherapy was begun, starting at five minutes and gradually increasing up to thirty minutes. The patient's room was so situated that the morning sun played directly into the wound and the afternoon sun was very nicely reflected on the wound by means of a mirror. Heliotherapy was discontinued on October 12 and the patient allowed to leave the hospital for his home in West Virginia. There was no elevation of temperature and he complained of no pain. The condition of the wound looked about the same as formerly reported, except that it was possibly slightly smaller. The grayish tenacious membrane was still present, and we were still unable to strap the edges together with adhesive. The wound looked indolent and indifferent but as if it would heal if it had a better blood supply. Never at any time during the four months of care had we seen a drop of blood, blood clots or any reddish discoloration on the gauze dressing. The skin remained bluish red, and for an inch or so back of the margins of the wound the tissues were greatly indurated and thickened, with here and there discrete, painless, hardened, subcutaneous lumps, which we took to be fibrosis of fatty nodules directly responding as a physiologic consequence to the use of the x-ray.

As the patient had been under our constant care for some four months, except for the short stay of a few days at Old Point, we were considerably discouraged that there should not have been more decided evidences of union and at least some effort for restitution on the part of the wound for closure. Letters were written to the doctors in Baltimore, who had previously treated him, asking for advice and suggestions. The reply was as follows: "Examinations here were negative, so far as metastases to the chest or osseous system were concerned. The nonprotein nitrogen and urea nitrogen were both high. Mr. F. had a four plus Wassermann reaction. In view of the possibility of malignancy in the ureter, we advised a ureterectomy. It seems to me that the local conditions in the pelvis might be due to the syphilis, or possibly the high nitrogen retention is interfering with the healing; or perhaps there is some remaining trouble which has extended from the ureter. I am very much interested to know what your microscopic examination showed as to the ureter. I have had, of course, a great many cases of tuberculous ureteritis where sinuses and difficulties in healing have persisted for months, or even years, but I don't remember ever having seen such a situation in connection with cancer."

It is interesting to note here that the Wassermann and Kahn tests on every occasion of examination at Stuart Circle Hospital were negative, quite in contrast to the findings reported in Baltimore. Nor did we find the nonprotein nitrogen and blood urea to be so concentrated as to be of any decided clinical significance.

An eminent radiologist, who was consulted, expressed himself as follows: "I believe that the best treatment for this man would be with the high voltage x-rays, preferably Constant Potential, at 211 K.V., using 2 mm. of copper filter, and treating the patient twice daily, alternating anteriorly, posteriorly, and perhaps laterally. Before attempting this, however, you should make an x-ray examination of his chest to determine whether you already have evidences of a general carcinomatosis. If so, this treatment over the local disease will not cure it, and will probably be wasted energy. A case of this kind requires the most constant detailed skilful treatment, and no one can lay down a definite rule for its treatment. The above are mere suggestions which may be helpful."

On December 9, 1931, the patient was examined again. The wound had filled in a very little in the previous two months. It still had the grayish tenacious membrane. It was being dressed by the patient twice daily with balsam of Peru and castor oil. The skin was of the bluish reddish congested color. The subcutaneous tissues were hardened, dense, indurated and more contracted than formerly as they did not pit on pressure. There was no pain, the patient was bright and happy, and had gained in weight. The sharp vertical para-rectus line of the protecting lead plate was still very evident, as was the horizontal one about the groin. There was continuance of the anhidrosis and absence of all hair.

Mr. F. remained at home through the winter doing a little work about his office, and in March again noticed a discoloration of his urine. A cystoscopic examination was made and the origin located in the bladder mucosa about the opening of the left ureter. Dr. William E. Lower, of the Crile Clinic in Cleveland, was invited to see him and the following excerpts are from his letter to me, dated April 13, 1932.

"Replying to your letter of April 11 relative to Mr. F., I saw him about two weeks before I operated upon him, and at that time found he had a metastasis in the bladder in the region of the left ureterovesical orifice. At the time of the operation, April 4, I resected this area of the bladder with what seemed to be about two inches of ureter, although this may have been more or less scar tissue extending up the course of the ureter. At any rate, the only metastasis seemed to be at the bladder. I inserted some radium emanation seeds in this area. There was also an ulcerated area in the old scar in the skin which had not healed, and this was resected and the wound left open and radium seed applied along the margin.

"His general condition seemed very good. We were unable to find

any distant metastases, and, while the outlook is not good, it seems to me that he has a fair chance of being quite comfortable for awhile, with the hope that we may be able to stop the progress of it, although, as you know, this is doubtful."

The convalescence and restitution of Mr. F. was slow following this operation. After having been confined to bed for several months he was later able to be up and about the house, with the encouraging evidence of increasing strength and weight, but on July 1, 1932, his physician was hurriedly called in. In a personal conversation with me, he gave the following details of another operation.

"Mr. F. was suddenly taken with acute abdominal distention and vomiting, with every indication of acute intestinal obstruction. He was carried to the hospital and operated upon immediately. A very highly organized Lane's kink was found producing an obstruction at the ileocecal valve. This contraction was so dense that a pair of forceps would hardly go through the opening. The constriction was incised but the distention of the intestines was so great that an enterostomy was performed. The hand put in the abdomen felt an enormous tumor apparently involving the sigmoid and descending colon, which by virtue of its size and location must be structures which are likewise malignant. Due to the enormous overgrowth there was likewise a partial obstruction of the large intestine but nothing further than an enterostomy was done for its relief. At this time an examination was made of the stomach and no ulcer or growth was located, so I am of the opinion that the heavily organized Lane's kink produced a pylorospasm, which in turn gave rise to the vomiting and gastric distress from which Mr. F. had suffered for so many years. There was very little bleeding at the time of the operation. The tissues were indurated, hard and the left rectus incision performed about a year previously is still open and not healed. He reacted nicely following the operation, and the tube drained well.

"Mr. F. had been improving up to the time of the emergency operation, although the left rectus wound was still open. He had no temperature; there was no herniation, but the tissues about the wound were hard and indurated, necessitating dressing daily. The acute abdominal condition was not due to the left tumor mass but to the organized Lane's kink."

The patient decided on the evening of July 14 to go to San Francisco to receive the Coffey-Humber cancer treatment. At the time of the trip he was carrying the colostomy tube, which apparently was working nicely, and he complained of no pain. He was taking very little nourishment other than glucose.

He arrived at St. Francis Hospital July 19 and died rather suddenly August 18, 1932. Dr. H. D. Humber sent me the following record of the autopsy.

"Autopsy performed by Dr. A. M. Moody, August 18, 1932. Bi-

lateral lobular pneumonia (terminal) and extensive fibrous peritonitis with multiple partial intestinal obstruction from adhesions between loops of the ileum, and between the colon and the abdominal wall; cecostomy on the right with suppurating wound in the anterior right abdominal wall; suppurating wound in left abdominal wall over descending colon, and fecal fistula with a deep abscess (about 30 cubic centimeters pus) between colon and left lateral abdominal wall; healed incised wound in left kidney region; x-ray pigmentation of skin region but otherwise unaltered.

"*Lungs*—Dependent portions edematous and there are rather extensive regions of lobular pneumonia in the lower lobes and right upper lobe, with an acute fibrinous pleuritis. *Liver*—firm and slightly shrunken. *Spleen*—relatively large anemic infarct with thrombosis of branch of sclerotic splenic artery. *Adrenals*—right contains small island of bone and left is hypertrophic. *Kidney*—compensatory hypertrophy of right (one and one-half times normal) with acute nephrosis. *Pancreas*—unaltered. *Prostate*—small and soft. *Bladder*—normal.

"*Note—there is no tumor found.*

"Principal cause of death—bilateral lobular pneumonia (terminal); fibrous peritonitis with incomplete bowel obstruction. Contributory cause—colostomy (right) and fecal fistula (left)."

The above case is of peculiar interest to me for the following reasons:

1. That he should have had a carcinoma of the kidney associated with no pain, hematuria or evident tumor, the three cardinal symptoms of kidney neoplasm, is certainly most unusual. The consideration of the pathology, course and surgery of renal malignancy cannot be taken up at this time.

2. His individual response to the x-ray had a most pronounced reaction in the obliterative endarteritis characterized by anemia, blanching and hardening of the tissues, by the generalized fibrosis in the subcutaneous structures and the evident discoloration of the skin, which, although controlling the malignant growth as shown by necropsy, had its untoward effects in marked tissue response and fibrosis with failure of union of the several abdominal incisions. I wonder if the day will come when the absolute dosage, the amount, the exposure and the penetration of x-ray therapeusis will be so accurately and biologically measured and adjusted to the individual sensitization and personal idiosyncrasy and response that its lethal effect on embryonal malignancy will be physiologically computed and foretold, thus avoiding the unfortunate reaction in the normal

tissue about the tumor so treated. This is simply a suggestion and comes from one who knows nothing about roentgenology.

3. It is a question in our opinion whether he ever had gastric ulcer! It was not discovered at autopsy. The pylorospasm was most likely due to the highly organized Lane's kink, or indeed to a chronic appendix.

4. That despite the several operations for the recurring carcinoma in the urinary tract—first, kidney, then ureter and then bladder—no evidences of malignancy whatever were found at autopsy. Surely the therapeutic influences of the x-ray are very dramatically illustrated.

The tumor mass in the left side noticed at his final operation, July 1, 1932, apparently involving the sigmoid and descending colon, which was naturally considered to be a malignancy, proved at autopsy to be a fecal fistula and abscess. This was at the location of my operation performed a year preceding. What had happened in the meanwhile to bring about such a condition of affairs? Was it an intra-abdominal diverticulitis from sigmoidal and colonic replacement fibrosis? an obliterative endarteritis with consequent necrosis? a prolonged anemia and ischemia from abdominal pressure? I do not know! But our operation was extraperitoneal and in no way encroached upon or embarrassed the colon. A marked blanching and whiteness was noted during our operation of all tissues about the course of the ureter.

5. That the disease had been pretty satisfactorily controlled is evidenced by the necropsy report, which showed no carcinomatous recurrence anywhere in the body, but there was an hypertrophy of the adrenals and doubtless the super-production of an autogenous cortin, or adrenalin by-product, which is, I believe, the theory upon which the Coffey-Humber treatment of cancer is based.

In talking over the necropsy findings of the suprarenals with pathologists I am informed that hypertrophy of the adrenals is constantly seen in prolonged toxemia and suppuration. The cecal abscess of the left side may then have been, and most likely was, the cause of the suprarenal response. Dr. Beck states, however, that there is no record of any case of which she knows in which an osseous degeneration has been found in a ductless gland such as the thyroid or adrenals. The most logical explanation is that the condition arose from an embryonic rest, or was some calcium deposits

in the fibrous tissue. This bony deposit, this small island, alone could be worthy of the attention and much study on the part of pathologists. Apparently this is something new and unknown.

Another very interesting and significant finding was that of the spleen, "a relatively large anemic infarct with thrombosis of a branch of sclerotic splenic artery." Again the far-reaching influence of the x-ray is noted—exposure, obliterating endarteritis, sclerosis. It was just in this location (on the left side) that the x-ray was used, and it was here that we find the dermal pigmentation and thickening, the subdermal fibrosis and anemia, the crenation and hardening, and the ischemia, the disappearing arteries (and that in a large artery, the splenic) and the abscess formation. Growth, life and function are contingent upon arterial blood! No such pathology was found in the right side, which received no x-ray treatment.

I have had the opportunity, as we all have had, to try out various recommended measures for the relief and cure of cancer somewhere in the body, among them those included in the following list:

1. Coley's fluid, one of the better known, is based on a response to the subcutaneous injections of the mixed toxins of erysipelas and bacillus prodigiosus.

2. Fulguration, electrocoagulation, electrotherapy, thermocautery, galvanocautery, x-ray and radium are too well known to dwell on here.

3. The use of lead, colloidal lead, colloidal gold, phosphate and manganese, irradiation of the blood, cancerous extracts, thymus extracts, insulin—3 units daily—endocrine preparations, ultrapeptones, and specific protein therapy are a few of the more recent therapeutic measures which have been tried out by various clinics and physicians.

How can we determine the biologic equation in malignancy of the response of the human body to drugs? Is it the medicine? Is it the turning point of the malignant invasion? Is it some unknown, undreamed of extraneous factor? Is it an autogenous vaccine? Are the bolsheviking cells finally coming to their pathologic senses and observing again law and order? There are no scales, no calipers, no measuring stick which infallibly and unalterably classifies malignant invasion, pronouncing the one fatal, lethal,

hopeless; the other curable. Each and all of us can recall such cases.

The individual equation, great personal intimacy and unusual professional interest which I had in this case, the multiple operations, emergency surgery, unhappy termination and striking necropsy report, have prompted me to report this history at length.

DISCUSSION

MR. J. SWIFT JOLY (London, England): Gentlemen, I should like to show you some slides of these villous tumors of the renal pelvis and I picked these out because they are cases in which one was able in most instances, practically in every instance, to make a diagnosis before operation. In a great number of cases, of course, it is extraordinarily difficult to distinguish between a villous tumor of the renal pelvis and a solid carcinoma of the kidney itself. Both give filling defects in the pyelogram and it is very hard to differentiate one from the other. These slides are just a few cases in which we were able to make a diagnosis beforehand.

(Slide) The first case I am showing you is interesting because the patient had no symptoms whatsoever of a renal tumor. He came into the hospital with an initial hematuria and, on uroscopy, villosity was found in the ureter. We then investigated him and found very large filling defects in the upper pole of the left kidney. The right side was quite normal. If you will look closely, you will see there is a definite outline to the lower border of that filling defect. We came to the conclusion there was a villous tumor springing from the upper pole of the kidney.

(Slide) This is another pyelogram with a slightly less, a smaller distention. It shows the lower edge of the filling defect very clearly.

(Slide) This is the kidney itself. The whole of the upper half of the kidney was replaced by an extensive villous tumor. All this portion is tumor, spreading down here into the renal pelvis, and you see the individual villi fairly well marked.

(Slide) This is a case of a man with pain in the loin. A plain x-ray showed a urinary calculus at that level and the pyelogram showed a very diffuse, very irregular defect, as though the opaque fluid had been absorbed in the pores of a sponge. I did a nephroureterectomy. We found a totally functionless kidney and there was a diffuse papillomatosis covering the whole of the renal pelvis and all of the calices.

(Slide) This is another case with calculus. There are two stones in the lower calix. The patient had very little hematuria, but the pyelogram shows a big, rather diffuse filling defect there.

As a matter of fact, all of this is a filling defect. It doesn't show, but that spotty nature of the filling defect is one of the characteristics of this condition. A nephro-ureterectomy was done in this case. This man developed secondary deposits in his bladder after the operation and he also had secondary deposits in the lungs and died about four years after his operation from their growth.

(Slide) This is the smallest villous tumor that we have been able to diagnose. The patient was a man who gave a very clear history of fifteen months' duration, hematuria associated with unilateral pain, pain in the right side or the left, I have forgotten which. In doing the pyelogram, the whole of the renal pelvis appeared to be normal except the extreme upper calix, in which there was just a little suspicion of a filling defect. He was an old man, well over seventy, so I simply did a plain nephrectomy on him. He had a tiny papilloma about the size of a pea in the calix and that was the only lesion we found.

(Slide) This is a ureterogram of a case in which a plain nephrectomy was done for tumor of the renal pelvis. You will see there is a catheter in the ureter there (indicating) and a filling defect due to a growth in the ureter there, and another filling defect there. Recurrent hematuria appeared about eighteen months after operation.

(Slide) This is another radiogram of the same case showing a defect there and a defect here after the catheter had been removed. These two slides were lent to me by Sir John Thomson Walker. He removed the ureter and I believe the patient then developed tumors in the bladder which were treated by cystoscopic diathermy and the last I heard the patient had been free from recurrence for about three years. I don't know whether you can see these defects. There are two quite large tumors in the ureter.

(Slide) This is an operation specimen of one of the secondary tumors of the ureter. You see the papillary masses there and a great mass here which was prolapsed into the bladder. A portion of the bladder around the ureter was also excised in that case.

(Slide) This cystoscopic pyelogram shows what is apparently a primary tumor of the ureter, of the extreme lower end of the ureter. It shows just a filling defect at that point. The ureter seems to be detached from the bladder and the renal pelvis does not show any defect at all. That was a case under the care of my colleague,

Mr. Barrington. The descending pyelogram showed exactly the same appearance.

(Slide) This is the last slide I show; it is simply the cystoscopic appearance of one of these tumors projecting through the ureter.

DR. RICHARD F. O'NEIL (Boston, Mass.): I should like to say a word in regard to the diagnosis of tumor of the renal pelvis and ureter from the pyelo-ureterogram. Filling defects in the pelvis and ureter may be due to the presence of blood clot and, if doubt exists, reliance should not be placed on one observation alone.

A recent case on my service well illustrates this: The patient had a massive hematuria with vesical retention due to clots; after these had been evacuated, the bleeding was found to be from one kidney. A pyelo-ureterogram was made which showed typical appearing filling defects in the pelvis and upper ureter, interpreted as being due to pelvic and ureteral growths. At operation a renal neoplasm was found involving a major calix, but there were no tumors of the renal pelvis or ureter, the filling defect having been due to blood clots.

DR. GEORGE R. LIVERMORE (Memphis, Tenn.): I would like to report progress on the case of papillary carcinoma of the renal pelvis which I reported before this Association in 1928 and on which I reported subsequent progress two years later. This man had a recurrence in his bladder of papilloma about the right orifice. The original tumor had been in the left kidney pelvis. Under fulguration, these tumors in the bladder disappeared. That was in 1928 and 1930. He has also had recurrences in 1931, 1932 and 1933 as well. All have disappeared under fulguration and deep x-ray.

He was at the office about three weeks ago, when he had a recurrence near the right ureteral orifice, a papillary growth about the size of the end of the index finger. Under fulguration this is sloughing away and when I saw him about three or four days ago, it looked as though it were going to come away in one piece.

DR. C. E. BURFORD (St. Louis, Mo.): I wish to discuss briefly three cases we reported at this meeting some years ago. Two patients had a nephrectomy done without a ureterectomy. In one of those, a man who was then sixty-eight and is now about eighty-three, the nephrectomy was done without the ureterectomy. He had no further symptoms until about a year ago when he had symp-

toms of urinary obstruction at the vesical neck. We found a rather hard prostate, did a resection and found carcinoma of the prostate. That is the only evidence of any possible metastasis in that case.

One of the other cases, in which we did a complete ureterectomy, taking out a section of the bladder, was that of a woman about forty years of age and we were able to remove the ureter and the section from the bladder without doing suprapubic cystotomy. However, in about six months following the ureterectomy, there was a recurrence of papillomata about the section from which we removed this piece of bladder. This was fulgurated and the woman recovered at the time, but some three years later died of pneumonia. We were unable to make a postmortem examination, but we think from the x-rays there were metastases in the lungs.

I wish to emphasize the fact that I believe it is necessary to do ureterectomy in all these cases and to remove a section of the bladder when the ureteral orifice is involved.

Dr. Bransford Lewis (St. Louis, Mo.): The tumor I wish to mention is not one of this classification, having been a hypernephroma, but it offers the opportunity of presenting the very cheerful record of our having relieved the patient now for twenty-two years. I operated in 1912, removing hypernephroma much larger than your doubled fist. He had already been bleeding more or less for six years. Twenty-two and six make twenty-eight years of history for that patient, but postoperatively twenty-two years. Now I understand that the patient is still alive and well. He is in California. I don't know whether the California climate has anything to do with it, but he is well and has renewed his regular vocation. Usually such patients die within two to five years after operation.

Dr. Henry L. Sanford (Cleveland, Ohio): I would like to report perhaps the opposite side of Dr. Bryan's experience. Four years ago we had a man with a bad hematuria, on whom we made a diagnosis of tumor of the kidney pelvis from a big filling defect in the pyelogram. But he had very evident metastases in the lungs and we told him that operation would be useless. On account of the fact that he was bleeding so badly and two or three transfusions hadn't helped him, he asked to have his kidney taken out, which we did. He recovered and had x-ray treatments over a long period. As we watched the successive x-ray plates, we could see that these puff-ball appearances in the lungs were disappearing.

I was called up by a life insurance company just the other day —that was four years after the operation—and the agent wanted to know if the man was a good life insurance risk. The man is working at present.

DR. JOSEPH HUME (New Orleans, La.): I want to call attention to one point that is not brought out very often, and that is the danger of getting transplantations of these papillary carcinomas by manipulations with the ureteral catheter. That should be borne in mind and manipulation should be limited as far as possible. I believe after such cystoscopic manipulation, the bladder should be filled with an alcoholic solution for at least three minutes to try to prevent any recurrence there.

DR. THOMAS P. SHUPE (Cleveland, Ohio): In the second case, classified as a transitional cell papilloma, there was no invasion of the resected renal pelvis and the attachment of the tumor to the pelvis was not over two millimeters in diameter.

HYPERPARATHYROIDISM AND RENAL DISEASE

WITH A NOTE AS TO THE FORMATION OF CALCIUM CASTS IN THIS DISEASE

FULLER ALBRIGHT, M.D. (by invitation), and ESTHER BLOOMBERG

From the Department of Medicine, Massachusetts General Hospital, Boston, Massachusetts

In a previous communication[2] the renal complications of hyperparathyroidism were divided into three types: Type I, where the kidney disease was secondary to extrarenal stone formation; Type II, where the kidney disease was due to calcium deposits in the intrarenal urinary passageways; and Type III, parathyroid poisoning, where the kidney was just one of several organs involved in a general precipitation of calcium.

The present communication concerns itself with three items: (1) the frequency of hyperparathydroism as a cause of stone formation, (2) some observations of diagnostic value on the urinary sediment of patients with hyperparathyroidism, and (3) a short discussion of the problem of stone formation in general as influenced by knowledge obtained from hyperparathyroidism.

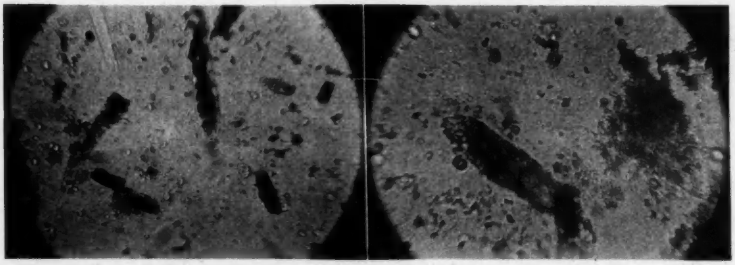
FREQUENCY OF HYPERPARATHYROIDISM AS A CAUSE OF RENAL STONE

There is no question that, given a case of hyperparathyroidism, renal calculi are apt to be present. Thus, in a series of eighty-three cases of hyperparathyroidism,[2] Type I renal lesions were found twenty-three times, and Type II lesions seventeen times. The question for the urologic surgeon in a case of kidney stone, however, is: how likely is it to be due to hyperparathyroidism? The question cannot yet be answered, except to say that there is enough chance of the condition being hyperparathyroidism that the attending physician should feel obliged to rule this disease in or out. The series of cases studied at the Massachusetts General Hospital is quite convincing in this respect. To date this series comprises twenty-three cases proved by operation. Of these cases, fifteen patients had renal calculi and three others Type II renal lesions. What is more important, however, is that eleven patients were suspected of having the

disease only because of the renal calculi and had no bone disease. It is to be noted that only five patients had bone disease without renal disease. The series suggests, therefore, that renal disease is a more frequent manifestation of hyperparathyroidism than is bone disease.

CALCIUM CASTS IN PATIENT WITH HYPERPARATHYROIDISM

Many fine granular casts were noted in the urinary sediment of patient 16 in the series (Fig. 1). They seemed all the more re-



A B

Fig. 1. *A.* Casts in a case of hyperparathyroidism as seen by "low power." The casts are in a transition stage between granular and hyalin due to the administration of ammonium chloride (see text). One cast in which the granules have been reabsorbed from the outside can be seen in the center of the field.
B. Same casts as seen by "high power." Note that structure is same as that of phosphate precipitates not in cast form.

markable since the urine contained no albumin or only the slightest possible trace. It was recalled that similar casts had been noted in previous patients without their having occasioned special attention. Further observation revealed that the granules themselves were all similar to each other and not unlike those of amorphous phosphates. They had the same almost black appearance which amorphous phosphates frequently give when seen microscopically in sediments.

It was then recalled that the kidney lesion in the Type II form of renal involvement consisted of plugs containings calcium, presumably calcium phosphate, in the tubules. Such a plug, if it became free and made its way to the kidney pelvis, would constitute a fine granular cast. In Figure 2 is depicted a microphotograph of

such a cast in a tubule of a rat with experimental hyperparathyroidism. The suggestion occurred that the granular casts seen in the urine of patient 16 might represent evidence of Type II renal damage in the making. Tests were devised to substantiate or disprove this point of view.

If the casts represented calcium phosphate deposits in a hyalin

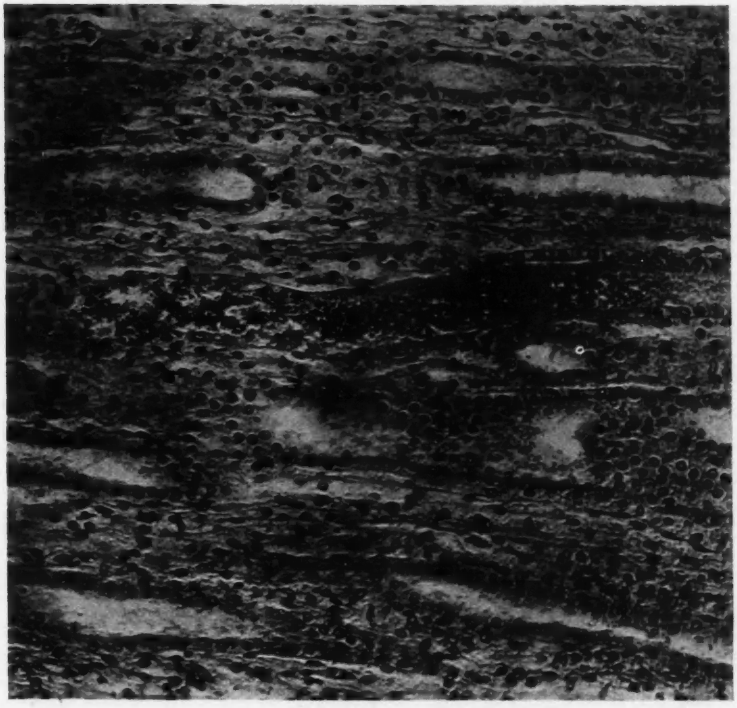


Fig. 2. Photomicrograph of kidney of rat which received overdosage of parathyroid extract. Cast can be seen in tubule. Black spots represent calcium deposits since preparation has been stained with von Kossa silver stain.

matrix, the granules should disappear on adding acid to the urine. This proved to be the case. If the casts contained calcium, they should stain black with the von Kossa silver stain which is specific for calcium. They did. If adding acid to the urine dissolved the

granules, a sufficiently acid urine as passed should prevent their formation. This was so, and was shown in the following manner. Hourly specimens of urine were taken before and after the ingestion of ammonium chloride. These were tested for specific gravity, pH (colorimetric method), and presence of the granular casts and amorphous phosphate crystals. The results are shown in Table I.

It will be noted from Table I that as the urine became more acid

TABLE I. SHOWING EFFECT OF pH OF URINE ON TYPE AND NUMBER OF CASTS

Date	Time	pH	Specific Gravity	Urinary Sediment			NH_4Cl
				Gr. Casts	Hyal. Casts	Phosphate Crystals	
2-10-34	10:45 A. M.	6.6	1.012	+++	0	++	1 gm.
"	11:45 A. M.	6.6	1.008	+++	0	++	1 gm.
"	12:45 P. M.	5.8	1.012	0	+++	0	1 gm.
"	1:45 P. M.	5.9	1.015	+	+++	0	1 gm.
"	2:45 P. M.	6.1	1.012	+	+++	0	1 gm.
"	3:45 P. M.	5.6	1.012	0	+++	0	
"	4:45 P. M.	5.5	1.014	0	+	0	
"	5:45 P. M.	5.3	1.014	0	+	0	
"	6:45 P. M.	5.4	1.008	0	+	0	
"	7:45 P. M.	6.1	1.010	0	0	0	
"	8:45 P. M.	6.1	1.013	+	+	0	
"	9:45 P. M.	6.2	1.005	+	0	0	
2-11-34	11:00 A. M.	6.9	1.008	+++	0	+++	
"	12:00 M.	6.6	1.008	+++	0	++	
"	4:20 P. M.	6.6	1.005	+++	0	++	

the granular casts became less and less granular until they turned into hyalin ones and then even these disappeared. With a return to a less acid condition the granular casts recurred. This could be repeated at will. The casts bore no relation to the specific gravity. After the operation of parathyroidectomy the casts disappeared regardless of the pH.

Since this experience these same casts have been noted in the urines of most of the subsequent patients with hyperparathyroidism. They are not pathognomonic of the condition, but occur in moderate numbers in some alkaline urines which are loaded with phosphates. Their presence in large numbers, however, especially if repeatedly so, should certainly make one consider the diagnosis of hyperparathyroidism. In short they offer evidence which is easy to obtain and which is at least suggestive of the disease. When they are present in large numbers, as they were in patients 16, 19, and 23, they should be considered a sign of the taking place of Type II renal damage.

The existence of such granular casts when the granules are due to calcium phosphate salts or phosphate salts of any kind is not commented upon in most clinical works. Addis and Oliver[1] state that "finely divided debris is the characteristic component of the granular cast" but do not further discuss the nature of the debris. Lubarsch,[4] however, gives considerable discussion to calcium casts in kidney tissue. They are found chiefly in connection with "calcium infarcts." These are not infarcts at all but calcium deposits in the kidney pyramids, in some instances just a conglomeration of calcium casts in this region. Such "infarcts" can be seen by roentgenogram on occasion. The patient with hyperparathyroidism reported first by Ettinger and Magendantz[3] and later by others[2] illustrated this point very well. Here the outlines of the pyramids of both kidneys stood out clearly because of the punctate deposits of calcium in them.

The casts are extremely fragile, which makes the obtaining of permanent preparations difficult. Just where the hyalin groundwork comes from is not clear. The following observations pertaining to this question should be emphasized. The granular casts change into hyalin ones as the urine becomes more acid. However, the fact that these hyalin casts soon disappear after this metamorphosis makes it quite clear that one is not dealing with the precipitation of calcium salts in hyalin casts which are being formed for other reasons. One is forced to conclude that the precipitation of the phosphates and the formation of hyalin ground structures are two processes which go on together and that the latter does not occur without the former. The granules, however, apparently can be reabsorbed on occasions.

INFERENCE AS TO STONE FORMATION IN GENERAL TO BE DERIVED FROM STONE FORMATION IN HYPERPARATHYROIDISM

The practical question in any one case where there is a tendency to form renal stones is not, what is the cause of the stone formation, but, what in that individual predisposes him to stone formation? Thus, in the patient with cystinuria and a pure cystine stone, it is obvious that the predisposing factor is the cystinuria. So in the patient with a tendency to form stones composed largely of calcium and phosphate salts and with hyperparathyroidism and, therefore, hyperphosphaturia and hypercalcinuria, it is obvious that the predisposing factors must be the increased excretions of these elements. This adds, therefore, another clear-cut example of a type of stone due to excess crystalloids in the urine. This in no way means, and it is entirely improbable, that excess of crystalloids in the urine is the cause of all stones, but it should direct attention more in that direction.

Three patients were encountered in the course of this study who also add weight to the increased crystalloid factor as a cause of stone formation. They all had phosphate stones; they did not have hyperparathyrodism; they drank large amounts of milk; and two of them took alkalis as well (cf. Sippy regime). Milk contains large amounts of phosphates; phosphates are excreted largely in the urine; they are less soluble in alkaline urines. A probable factor in these cases was the hyperphosphaturia coupled with the alkaline urine. The question immediately is asked why everybody on the Sippy regime does not have stones. The same question could be asked regarding hyperparathyroidism. This cannot be answered. It may be that normal individuals vary with regard to the colloid content of their urine and only those with small amounts get stones when confronted with excessive crystalloids in their urine. As regards hyperparathyroidism, in the series of cases at the Massachusetts General Hospital there has been a tendency for the polyuria of this disease to be less marked in the patients with stones. Polyuria, of course, would be a protective mechanism as far as stone formation is concerned and its extent certainly has individual variations.

The studies reported above on the formation and dissolution of calcium phosphate casts may have some bearing on stone formation.

These structures, after all, are not unlike small stones. They consist of a hyalin ground material in which are deposited crystalloids. The factors concerned in their formation are the concentrations in the urine of calcium, of phosphate, and of hydrogen ions. There seems no reason to believe that the urinary colloids are decreased in hyperparathyroidism. It is not unlikely that the same factors which influence the formation of these casts, likewise influence the formation of the stones in the larger urinary passageways, notably the renal pelves.

CONCLUSIONS

1. Hyperparathyroidism is a sufficiently frequent cause of renal stone formation that its presence must be ruled in or out in every case of this disease.

2. Eleven cases are cited from a series of twenty-three proved cases of hyperparathyroidism at the Massachusetts General Hospital where the presence of renal stones was the only clue which led to the diagnosis of the underlying disease.

3. A frequent finding in hyperparathyroidism is the presence of many finely granular casts in the urinary sediment. The granules have been shown to contain calcium, probably calcium phosphate. The casts can be made to change into hyalin casts as the urine is made more acid by the giving of ammonium chloride by mouth. Their continuous presence in large numbers is an indication that intrarenal damage is in progress.

4. Probably the factors governing the formation of these casts, which in a way are microscopic calculi in the renal tubules, are the same which govern stone formation in hyperparathyroidism. These factors are the concentrations in the urine of calcium, of phosphate, and of hydrogen ions.

5. Stone formation in hyperparathyroidism belongs to that etiologic group where the presupposing abnormal factor is an excess of crystalloids in the urine. This fact is justification for further attention to this line of approach in the solution of the stone problem in general.

BIBLIOGRAPHY

1. Addis, T., and Oliver, J.: The Renal Lesion in Bright's Disease. Paul B. Hoeber, New York, 1931.

2. ALBRIGHT, F., BAIRD, P. C., COPE, O., and BLOOMBERG, E.: Studies on the physiology of the parathyroid glands. IV, Renal complications of hyperparathyroidism. Am. Jour. Med. Sci., 187:49, 1934.
3. ETTINGER, A., and MAGENDANTZ, H.: Roentgen evidence of extensive calcification of the kidneys in osteitis fibrosa cystica. Am. Jour. Roent., 331:593, 1934.
4. LUBARSCH, O.: Handbuch der Speziellen Pathogischen Anatomie und Histologie. Band VI, Erster Teil, S. 567.

SOME NEWER CONCEPTIONS OF URINARY STONE FORMATION

J. DELLINGER BARNEY, M.D., F.A.C.S.
and
E. ROSS MINTZ, M.D. (by invitation)
Boston, Massachusetts

This communication concerns itself primarily with a discussion of hyperparathyroidism as a cause of urinary calculi. In the course of our remarks certain other possible etiologic factors will be dealt with.

Next perhaps to malignant disease, urinary lithiasis presents one of the most difficult problems confronting the urologist. Until this question is answered he finds himself occupied in the more or less unproductive occupation of discovering and removing stones from kidney, ureter or bladder. We do not hesitate to say that no hypothesis as to etiology yet presented can be defended from every line of attack, nor does it matter that certain experimental studies have resulted in stone formation. What may be true in the laboratory does not necessarily follow in the clinic. Even parathyroid disease, which is found to be the apparent etiologic factor in at least 10 per cent of cases, brings up questions which in the present state of our knowledge cannot be answered.

It will be impossible for us to discuss and summarize the vast literature of urinary lithiasis. Until recently it was based only on clinical observation, theorization and empiricism. Only in the past ten, or even five years has anything been done by investigators with the lamp of modern biochemistry and physiology to light their path. Even so far as we have gone now it is obvious that the knowledge of neither the biochemist nor the physiologist is such that he can explore the even more complicated problems which have already arisen.

In the light of the work of Keyser, Joly, Higgins, Hinman, McCarrison, Randall, Holmes, Coplan, and others, to mention only a few, we have nothing new to add except our experience with hyperparathydroidism. We do feel, however, that long continued and intensive clinical observation, careful reading of the literature, and intimate contact with our colleague, Albright, who has done

epochal work, enable us to express views which will at least provoke further discussion.

Before going on to a consideration of the etiologic importance of the parathyroid gland, we wish very briefly to touch upon other possible factors in the production of stone. We believe with others that the colloids of the urine play an important rôle, and that whatever "brings about imbalance in the solvent capacity of the protective colloids . . ."[3] may result in crystalline deposits. Keyser seems to feel that at least in the formation of the so-called primary stones without infection, "some error of metabolism" occurs. In addition to this there would appear to be some disturbance of the normal physiology of the kidney which induces the formation of stones in one organ rather than in both. If, in the presence of a stone in an acid urine, infection occurs, especially by a urea-splitting organism, we may expect changes in the character of the stone; one layer or the nucleus itself being that deposited in the presence of the acid, sterile urine, another laid down by the infected alkaline urine. It seems to be a fact that the chemical character of the stone which occurs in or as a result of infection is very different from that in a clean and acid urine. Yet one must not forget that in various reported series of renal stones, some of them of the so-called secondary variety, investigators have found a persistently normal, uninfected urine in from 10 to 20 per cent of cases.

When one considers the various dietary and vitamin deficiencies, one finds so much contradictory evidence, both clinical and experimental, that in the present state of our knowledge it is impossible to draw any accurate conclusions. That these deficiencies are of some, if not great, importance no one can deny, nor can it be denied that their geographic distribution is of significance. A great deal of most intensive study must yet be brought to bear on these phases of the situation before we shall know how to interpret their meaning.

While infection plays its part, we know comparatively little about it. We find here also much conflicting evidence as to whether it is a primary or secondary occurrence. It seems to be clear, however, that it may alter the composition of the stone in a variety of ways, but just what goes on still remains to be discovered. Under the same caption faulty drainage can be included, but rather quickly dismissed, as an item of importance. While it may induce or in-

crease infection, we all know that it may continue almost indefinitely without resulting in stone formation. Yet neither of these factors, especially infection, can be allowed to continue if we are to lessen the chance of calculus deposits.

It is obvious from all this that many factors are undoubtedly at work, and that each must be evaluated. As Randall has wisely said, "The cause of stone must vary, for the effect is known to be a variant."

When the answer to all these questions has been discovered we shall know why stones form, why they vary in their composition, why they occur in one kidney and not in the other, why after removal they may recur in some instances (variously estimated as from 5 to 20 per cent) and not in others. It may also tell us why children are for the most part so free from stones.

Having dealt with the negative side of the question, we wish now to take up the positive side and narrate some of our experiences with parathyroid disease in its relation to stone. From various communications, especially those of Albright, Aub and Bauer, we know that disturbance of the parathyroid has a very far-reaching clinical effect. In their most recent article[1] they have discussed at length the extraordinary variety of symptoms to which hyperparathyroidism may give rise.

As our knowledge of and interest in this disease extends over only a comparatively brief period, we have used our material only for 1933 and 1934 to date. During this time 104 patients with urinary calculi having a complete blood examination for calcium and phosphorus, in some instances more than once, have been operated upon and stones removed. This number does not include a similar number in whom the bloods were not investigated. In twenty patients marked for re-checking the results proved to be negative in seven. Four of the remaining thirteen, not yet re-examined, would appear definitely to be instances of parathyroid disease if the blood findings are to be depended upon.

Our interest lies, however, in a group of eighteen patients with hyperparathyroidism, so proved by operation, eleven (61.1 per cent) of whom had not only parathyroid tumor, but also urinary calculi. These eleven cases are included in the 104 previously mentioned, giving a total percentage of 10.5. As already stated there

are other cases in this group which may prove to be positive, thus increasing this percentage very appreciably.

These eleven patients, all bearing stones, together with seven others, having no stones but cystic degeneration of the bones, have all been operated on by Dr. E. D. Churchill and Dr. Oliver Cope at the Massachusetts General Hospital, creating, we believe, a unique experience for all concerned. A report of some of this work has already been made.[2] In most cases with lithiasis the parathyroidectomy followed the lithotomy.

It is interesting to note that of the eighteen cases twelve (70 per cent) were in the female. The youngest patient was thirteen, and the oldest sixty-two, with an average age of forty-three. The calcium blood content varied from 11.5 to 16.8 with an average of 13.78; the phosphorus content averaged 2.55, ranging from 1.4 to 4.7. It may be remarked that a serum calcium above 11 mgm. per 100 c.c. and a serum phosphorus below 3.5 mgm. should always arouse suspicion. Bone involvement, ranging all the way from large, multiple cysts to simple decalcification, was found in twelve (70.5 per cent) cases. In six cases stones and bony changes were found together. The stones were bilateral in four (36 per cent) of the eleven cases, and the urine was negative in 35 per cent. There has been no operative mortality. One patient, however, died in the hospital about one month after his seventh operation, at which time the parathyroid tumor was discovered behind the sternum and was removed by Dr. E. D. Churchill. The cause of death was uremia, the direct result of parathyroid disease. The urologic surgery of these cases was done by various members of our staff.

We have given the details of these cases, not because, so far as the urologist is concerned, they differed in any way from other cases of urinary lithiasis, but because they were associated with parathyroid disease and because of this are highly interesting and important. Papers by Albright and by Churchill and Cope already published, or to appear later, describe in detail the medical and surgical problems encountered.

Our interest in this problem led us to a careful follow-up of as many of our cases of urinary lithiasis as we could recall. In all these cases operation has been performed and stones removed. Up to date thirty-three patients have been examined personally, this examination including the calcium and phosphorus blood content

and roentgenogram. Of this number eleven (33⅓ per cent) have the high blood calcium which is so consistent with parathyroid disease, and although in some of these the phosphorus content is rather high they must all be checked up and studied even more minutely. In only two cases, however, do there appear to be any bony changes. As yet no really complete follow-up has been done on the proved hyperparathyroid cases. This will be done in due course and a report made.

It will be noticed that we have said nothing about the chemistry of the stones removed in these cases of parathyroidism. As Albright, Aub and Bauer have pointed out, "If the stone is the result of hyperparathyroidism, it should contain a large amount of calcium and phosphorus." And in fact this is the case. We are not yet prepared to remark on the chemistry of these stones for the reason that no great amount of data is yet available, and also because it is to be reported at later time by Albright and his coworkers. Experience has shown that the proper study of these calculi can be done only by a highly-trained physical chemist. We believe that such an investigation may throw much valuable light on the etiology of calculi in general.

Not only our experience but that of many others has shown the close and frequent relationship of urinary calculi and parathyroid disease. A perusal of the literature, while by no means exhaustive, has been illuminating. Hunter in 1930 (Lancet, 1:897, 1930) collected thirty-two cases of osteitis fibrosa where satisfactory proof of hyperparathyroidism existed. In ten of the thirty-two cases (31.2 per cent) renal calculi were found. In one instance renal calculi began to break up a few weeks after the removal of the parathyroid tumor and were passed into the bladder. Sixty-five cases of parathyroid disease have been reported by thirty-six other authors. Stones were present in fifteen (23.07 per cent), these being bilateral in ten (66 per cent). While many other cases of hyperparathyroidism have been reported by other investigators, we have considered only those which were more or less associated with urinary lithiasis.

From all that has been said it is obvious that we are dealing with a factor of the utmost importance in the etiology of stone. Whether the whole story has yet been told we doubt very much. The discovery is to be developed still further, and during this

process it may shed light on other phases of the calculus problem. As yet it does not answer all of the questions. If hyperparathyroidism is in the nature of an endocrine dysfunction, it must be generalized throughout the body and the urinary tract. Why then does it not result in stones in all cases or in bilateral stones uniformly? The fact that it does not would indicate that there must be some still unknown factor at work in the kidney itself which prevents stone formation in some cases. By the same reasoning there must be a local renal factor which induces unilateral stone in certain individuals and bilateral stones in others.

Perhaps a still more intensive study of the colloids will supply the answer. Possibly dietary and vitamin deficiencies or errors will be found to play their part more than seems now to be the case. Also it may be possible that infection or even stasis will come to be regarded more seriously. That some disturbance of metabolism plus a factor or factors existing at least temporarily in one or both kidneys is at work seems a plausible working hypothesis. The realization that hyperparathyroidism will account for at least a part of the problem is important and encouraging. Further studies by the endocrinologist and the biochemist, as well as by the physiologist will, we feel sure, eventually succeed in solving the question of urinary stone formation.

REFERENCES

1. ALBRIGHT, AUB and BAUER: Jour. Am. Med. Assn., (April 21) 1934.
2. CHURCHILL, E. D., and COPE, OLIVER: Surg., Gynec. and Obstes., (Feb.) 1934.
3. KEYSER: So. Med. Jour., (Oct.) 1932.

ANURIA AS A COMPLICATION OF LITHIASIS

J. SWIFT JOLY, M.D., F.R.C.S. (by invitation)
Senior Surgeon to St. Peter's Hospital for Stone, London, England

Anuria is a symptom of a number of diseases, some of which are primarily unconnected with the urinary tract. It should never be considered as a disease itself. The conditions giving rise to anuria are so numerous that cases exhibiting this symptom are usually classified in three groups. The first group comprises cases in which the abolition of the excretion of urine is due to some general cause, usually a change in the blood circulation. Advanced cardiac disease, a marked fall of the blood pressure, or a local interference with the renal circulation (pressure of a new growth or an aneurism on the renal vessels) are all examples. Such cases are called prerenal anurias. The second type is called a renal anuria, and is caused by some change in the renal parenchyma, which renders it incapable of excreting urine; poisoning by corrosive sublimate being the most typical example. In the third group, the urine is dammed back in the urinary passages so that none of it can escape. This form is called a postrenal or obstructive anuria. All these types of anuria are encountered as complications of lithiasis, and the object of this paper is to indicate, as far as possible, to what extent they are individually responsible for the cessation of the excretion of urine.

UNILATERAL ANURIA

Before considering the cases in which no urine is eliminated, I wish to mention unilateral anuria. Cases of this condition are, I believe, not infrequent. One kidney is completely obstructed by a calculus, but the condition is masked by the continued secretion from the opposite organ. It is important, however, to recognize them, as the fate of the obstructed kidney depends on a prompt removal of the calculus. An unrelieved obstruction always results in the death of the kidney.

The following case serves as an illustration.

J. S., male, aged sixty-one, was first seen in the Out-patient Department of St. Peter's Hospital May 2, 1932. He had passed numerous

stones since 1914; two six weeks before examination. For the last week he had had severe pain in the right loin, radiating to the groin, accompanied by vomiting. He had noticed a marked diminution in the amount of urine passed since the attacks commenced, and felt weak and giddy. There was no hematuria; no pain on the left side. Cystoscopy in Out-patient Department revealed a right ureteric orifice rigid and gaping. No efflux was seen. The left ureteric orifice was normal, with normal efflux. The right ureter was catheterized to 28 cm., but no urine was withdrawn; suppression.

Examination upon admission May 5, 1932, revealed a stout, florid individual. The tongue was rather dry. There was tenderness on pressure in the right iliac fossa. Neither kidney was palpable or tender. Urine was turbid, neutral, sp. gr. 1008. There was a trace of albumin, small quantity of pus, few red blood cells, a few Gram-positive cocci. Daily urea was 1.7 per cent in 1,200 c.c.; blood urea, 60 mgm. per 100 c.c. Radiograms revealed a right ovoid ureteric calculus, level of transverse process, fifth lumbar vertebra. There was a large triangular shadow in the left renal pelvis, and a group of small shadows 1 inch external to it. Uroselectan B. urogram. There was no excretion on the right side for forty minutes. Right side, hydronephrosis—renal type, good excretion in ten minutes. Cystoscopy showed no excretion on the right side, normal efflux on the left. Bilateral catheterization was done to 25 cm. There was good flow from the left ureter; only a few drops from the right.

Examination of specimens: Right kidney, urine turbid from blood, neutral, sp. gr. 1015, quantity too small to estimate urea, pus in small quantity, few Gram-positive cocci.

Left kidney, urine slightly turbid, neutral, sp. gr. 1012, urea 1.8 per cent, pus in small quantity, Gram-positive cocci. Cultures (both sides) showed mixed growth of B. coli and micrococci.

Operation was performed May 9, 1932. Right ureterolithotomy was done, using oblique anterior incision. Stone was found at brim of pelvis, about 1 by 0.5 inches in size. Much uro-pus escaped after removal of stone. Convalescence was uncomplicated.

The patient was readmitted July 17, 1932. He had been well since the last operation and was putting on weight. Urine was as before; blood urea, 28 mgm. per 100 c.c. Uroselectan B. urogram. Right side showed good excretion in five minutes. Outlines of ureter and pelvis were normal. Left side, as before.

Operation consisted of a left pyelolithotomy. The renal pelvis was incised posteriorly. One large and six smaller calculi were removed. Convalescence was normal.

Pathologic report.—Both renal and ureteric calculi were composed of pure phosphates.

The patient was seen in Out-patient Department December 5, 1932. He had suffered from backache at times, and had passed gravel.

There were no other urinary symptoms. Urine was hazy, acid and showed a trace of albumin, few pus cells, and red blood cells. No organisms were seen. Sterile on culture. Radiograms showed no indication of stones.

In this case, the right kidney was not functioning at the time of the first operation, but was, if anything, the better of the two at the time of the second. If the obstruction had not been relieved, or if there had been an undue delay in doing so, it would have suffered irreparable damage. Results of experimental ligation of the ureter tend to show that a compleete obstruction lasting for more than two weeks is fatal to the kidney. In connection with this point, the experiments of Hinman and Morison are particularly interesting. They found that when one ureter was obstructed for less than a fortnight the kidney usually recovered, but if the obstruction was allowed to remain for three weeks the kidney atrophied unless its fellow was removed. This is a good example of "renal counterbalance." When one kidney is rendered functionless for three weeks, its fellow hypertrophies. There is then no stimulus to make it resume work. Removal of the unaffected organ provides the necessary stimulus.

In the case described above, the unobstructed kidney was gravely affected. The raised blood urea showed that it was incapable of eliminating the waste products of the body, although the urinary excretion was fair. The obstructed organ had, therefore, a decided stimulus to recover after operation, although its ureter had probably been blocked for a fortnight. I feel sure that if operation had been delayed, it would have atrophied, and that the patient would have gone down hill.

Excretion urography has given us an extremely easy method of diagnosing a unilateral anuria. It is more accurate than catheterization of the ureters, as non-drainage may be put down to the catheter blocking or to leakage of urine beside it. With excretion pyelography one may conclude that the kidney is functionless if there is no increase in density of its shadow, and no evidence that the dye has reached the renal pelvis. In such cases, the urogram of the obstructed organ is exactly similar to a plain radiogram.

Unilateral anuria is an urgent indication for operation. No time must be lost if the kidney is to be saved. This is important when

the calculus is unilateral, but it is even more important in cases of bilateral stone.

COMPLETE ANURIA

There are two types of complete anuria complicating lithiasis. The first is the obstructive type, in which the cessation of excretion is primarily due to the mechanical action of a stone or stones blocking the urinary passages. This form is commonly called "calculous anuria." In the second type there is no obstruction, but the renal parenchyma is so much damaged by the presence of calculi, usually associated with sepsis, that it is no longer capable of excreting

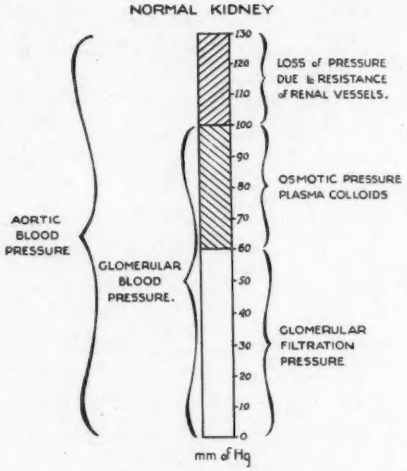


Fig. 1

urine. In cases of this nature the anuria is usually terminal, is uninfluenced by treatment, and is preceded by a long period in which the patient shows the classical signs of renal failure. Legueu[15] draws a sharp distinction between these two types; he calls the first "anurie par calculs," and the second "anurie avec calculs." This graphic nomenclature helps us to make a clear distinction between the two forms.

Calculous anuria is by far the most important type of complete anuria occurring with lithiasis, as it is amenable to treatment. The

kidneys are not destroyed, but excretion is inhibited, and they can resume their function once the obstruction is removed.

Cases of calculous anuria may be divided into three groups according to the nature of the obstruction. They are:

1. Obstruction of both kidneys or ureters.
2. Obstruction of the only functioning kidney.
3. Unilateral obstruction.

(1) *Obstruction of both kidneys or ureters.*—In this group both sides must be obstructed simultaneously, or almost simultaneously. If one kidney was obstructed a considerable time before the other, it would have become permanently functionless, and the case would come under the second group. The criterion for putting a case into this class is that both kidneys must be capable of resuming function when the obstructions are removeed. This group is probably the best example of a purely obstructive anuria.

In about three-fourths of the cases, stones are found in both ureters; in one-eighth, there are calculi in both renal pelves; while in the remaining eighth, a kidney stone on one side is associated with a ureteric calculus on the other. In addition, the upper portion of the ureter is usually involved, so that in most cases the stone can be removed through an ordinary kidney incision. The calculi are generally small, in fact a large stone is usually non-obstructive.

(2) *Obstruction of the only functioning kidney.*—In this group one kidney is obstructed, while its fellow is either absent, or is entirely destroyed by disease. Congenital absence of one kidney is an exceedingly rare occurrence, it is found about once in 2,500 cases (Morris). More recent statistics give a higher proportion. Gruber quotes statistics from various authors, which when added together give the proportion of one in 1,300 cases. The highest figures are given by Guizetti and Pariset[12] and by Engel.[6] In both these series, the proportion is approximately one in 500. Yet in spite of this rarity Eliot[5] was able to collect eighteen cases of calculous anuria in cases of congenital absence of one kidney, and since then Papin has been able to add six more. Unfortunately, Rubritius,[19] in his large collection of cases of anuria, does not discriminate between a solitary kidney after nephrectomy, and a congenital single kidney.

Anuria due to obstruction of the sole functioning kidney, its fel-

low being totally destroyed by disease, is not uncommon. Eliot collected nineteen such cases, and Caulk[8] found that eight out of sixty-one cases of calculous anuria were of this type. The most common lesions found in the non-functioning organ are pyonephrosis, tuberculosis (either complete caseation or an occluded kidney), and an extreme degree of hydronephrosis.

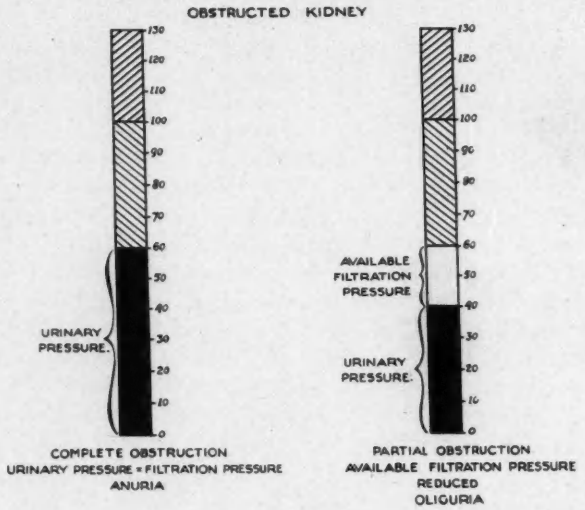


Fig. 2

Anuria from obstruction of the remaining kidney after nephrectomy is much more common than either of the preceding forms. Eliot collected twenty-nine cases of this type, and Gottstein[9] has added eleven more, but these figures underestimate its frequency. Caulk found a solitary kidney in fourteen out of sixty-one cases of calculous anuria, and Rubritius 113 out of 298. These figures show that in about one-third of all the cases there is only one kidney. This, however, includes cases of congenital absence as well as of surgical removal of one organ.

It is interesting to note that in eight of the thirty cases collected by Eliot and Gottstein, the anuria commenced within a month of the nephrectomy. It is probable that the obstruction was caused by

an unrecognized stone in the apparently sound side which was present at the time of the operation. Usually, however, the anuria occurs months or years after the nephrectomy, and is then due to fresh stone-formation. In at least three-quarters of the cases, the kidney was removed for lithiasis (usually calculous pyonephrosis), while tuberculosis was the next most common indication for operation.

(3) *Unilateral obstruction.*—The chief interest in this form or anuria is centered round two points: (1) the state of the unobstructed kidney, and (2) the reason why it has ceased to funtion.

There is no doubt that formerly many cases were described in which the unobstructed kidney was said to be healthy on insufficient

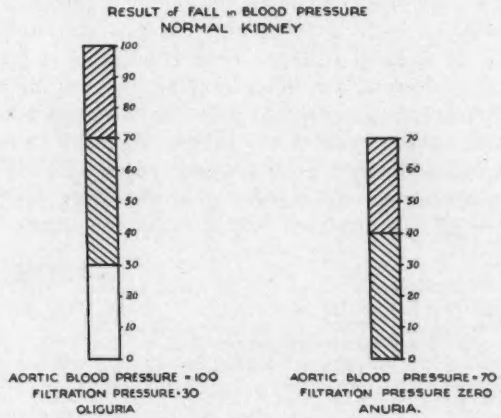


Fig. 3

grounds. In fact if no stone was found the organ was assumed to be healthy. Legueu[15] examined this question in 1890, and came to the conclusion that in thirty out of thirty-one cases published up to that time in sufficient detail, the unobstructed kidney was obviously diseased. In these cases the conclusions were based either on postmortem examinations, or on inspection of the organ exposed during operation. He stated that "one has never seen calculous anuria produced with a healthy kidney, that exceptionally the lesions of this kidney are trifling, but as a rule they are well marked."

On the other hand I believe that anuria can occur when one kidney is apparently healthy, but, as in such cases the condition is rarely if ever fatal, one must depend entirely on the examination of the urine, and the results of renal function tests carried out after excretion has been re-established. I also believe that it occurs only when pain is a marked feature. If the obstruction gives rise to severe pain, there may be a total cessation of excretion lasting as long as it is allowed to persist. If the pain is relieved, the excretion becomes automatically re-established. When the unobstructed kidney is diseased, a much slighter degree of pain is sufficient to give rise to anuria. In fact, the less efficient this organ is, the slighter the pain necessary to cause anuria. In the preceding types, all the renal tissue was put out of action by the mechanical obstruction, and in these pain is often absent or is an insignificant factor. When the calculus blocks off only a portion of the available kidney tissue, pain is always a marked feature of the condition. I lay stress on this point, as I think it affords an explanation of the manner in which a unilateral obstruction can give rise to bilateral anuria.

The relative frequency of these different forms of calculous anuria seems to have changed during recent years. This is very noticeable if we compare the figures given by Rubritius[19] in 1926 with those of Eliot in 1910.

Rubritius	Number	Per cent
Bilateral obstruction	88	24.8
Unilateral obstruction—		
Opposite kidney diseased	44	12.4
Condition of opposite kidney unknown	53	14.9
Opposite kidney wanting	113	31.8
Reflex anuria on opposite side	57	16.1
Total	355	

Eliot	Number	Per cent
Bilateral obstruction	64	42
Obstruction of only functioning kidney	69	45
Unilateral obstruction	19	13
Total	152	

Both tables agree in showing that calculous anuria is most commonly caused by obstruction of a solitary kidney. This type accounted for 45 per cent of Eliot's cases, and for only 31 per cent of those collected by Rubritius. Bilateral obstruction was found in 42 per cent of the older series (Eliot), and in only 24 per cent of the more recent. Perhaps the most striking change is the in-

creasing proportion of cases in which a partial obstruction gave rise to anuria. In Eliot's table 13 per cent were of this nature, while they form no less than 43 per cent of the cases collected by Rubritius. It must, however, be remembered that in a large proportion of Eliot's cases the disease was fatal, while this does not appear to hold good in Rubritius's series. This tends to confirm the opinion that calculous anuria is much less dangerous in cases of partial than of total obstruction. In fact, I believe that it is never fatal when the unobstructed kidney is normal, and that Legueu's dictum would have been correct if he had inserted the word "fatal." This question is still *sub judice*. It is, of course, extremely difficult to prove a negative, but I have yet to hear of a fatal case in which the unobstructed kidney was proved to be normal on microscopic examination.

REFLEX ANURIA

The term *reflex anuria* has become so common, and is used so extensively, that one is apt to forget that it depends, first, on the existence of a reflex arc from one kidney to the other, and, secondly, on whether the unobstructed kidney is inhibited through the nervous mechanism or in some other way. If either of these postulates is incorrect, it is obvious that the term itself should be abandoned.

The discussion over reflex anuria has lasted for more than forty years, and as yet there is no unanimity of opinion. Guyon, Albarran, Israel, and most of the urologists of the Vienna School were supporters of the theory of reflex anuria, while Morris, Legueu, Kümmell, Fahr, and many others opposed it. The weak point on the part of the opponents to the theory was that, although they were able to put forward weighty arguments against it, they never propounded a satisfactory alternative to it. I believe that such an alternative exists.

It is now generally accepted that the excretion of urine is essentially a double process: filtration and selective absorption. The glomeruli are simply filters, which hold back the colloids of the plasma, but allow water and crystalloids to pass through Bowman's capsule into the expanded upper extremities of the uriniferous tubules. The action of the tubules is to absorb water and certain substances such as chlorides and sugar, which are of use in the economy. They do not absorb bodies such as urea and sulphates,

which are entirely waste material. The first group are called the "threshold" substances, and are only eliminated when they are in excess in the blood stream. The second group are called the "non-threshold" substances, which are entirely eliminated. Recent investigations tend to show that the tubules have a certain power of excreting non-threshold substances, in addition to their chief function of absorption. This, however, is a comparatively minor function.

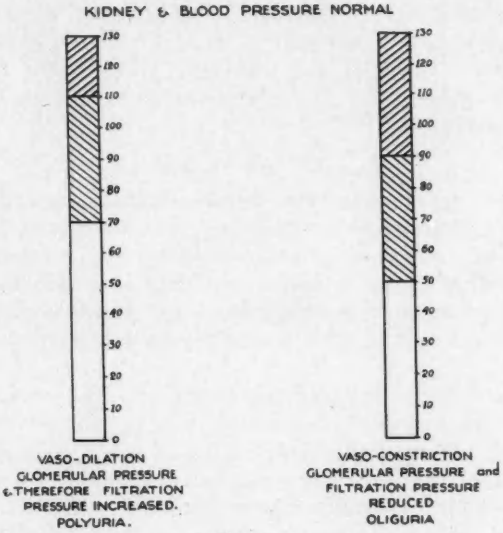


Fig. 4

Now, the speed with which any filter acts depends on the permeability of the filtering membrane, and the difference of pressure on either side of it. The kidney filter is composed of an exceedingly thin membrane, formed of the capillary walls and the exceedingly thin Bowman's capsule. It is, therefore, well suited for the purpose. The difference of pressure on the two sides of this membrane is very great. If we assume that the aortic blood pressure is 130 mm. of mercury, that of the glomerular vessels is about 100 mm. This extraordinarily high blood pressure in capillaries is not encountered elsewhere in the body. The pressure in the unob-

structed glomerular space is practically nil, and may be neglected, so that there is a difference of pressure of about 100 mm. of Hg. on the two sides of the filter. However, the whole of this pressure is not available for filtration. Starling has shown that the osmotic pressure of the plasma colloids is about 40 mm. of Hg., and, as this pressure opposes filtration, the total available filtration pressure is about 60 mm. of Hg.

If a cannula is tied into the ureter and connected with a manometer, one finds that the pressure steadily rises until it reaches about 60 mm. of Hg. It then remains constant as long as the general blood pressure is unchanged. It falls when the general blood pressure is lowered, and rises when the latter is increased. In fact the urinary pressure follows a curve which is similar to that of the aortic blood pressure, but is about 70 mm. of Hg. below it.

Stimulation of the nerves of the renal pedicle may alter this difference in height between the two curves, but does not influence their similarity. The renal nerves are vasomotor. A mild stimulation produces vasodilation, while a strong one causes constriction of the blood vessels. Vasodilation of the renal blood vessels decreases the difference in the abscissæ between the two curves, and may be considered as raising the curve of the urinary pressure nearer to that of the aortic blood, while vasoconstruction has the opposite effect.

No special secreto-motor nerves have been demonstrated for the kidney, similar to those of the submaxillary gland, for example. Stimulation of the chorda tympani nerve causes a copious flow of watery secretion from the submaxillary duct, and at the same time dilates the blood vessels of the gland. If a cannula is tied into the duct, the pressure registered by a manometer connected with it may exceed the carotid blood pressure while the chorda tympani is stimulated. This shows conclusively that the secretion is under nervous control. The renal excretion is, on the other hand, not under nervous control of this type. It can be carried on in a perfectly normal manner when the kidney is completely isolated from all nervous impulses. The experiments of Carrel and Guthrie,[1] which have been confirmed by Quinby,[18] have proved this point. Kidneys that have been excised, and reimplanted either into the same or another animal, can function satisfactorily. The only deviation from the normal is that at first there is a certain amount of hyperfunction,

due to absence of vasoconstriction, but this gradually passes off as the vessels recover their tone.

Again, the kidney cannot be compared with the pancreas, which is stimulated into activity by the presence of hormones in the blood. They are created by the action of the acid chyme on the duodenal mucous membrane, are absorbed into the circulation, and excite pancreatic secretion when they reach the gland via the blood stream.

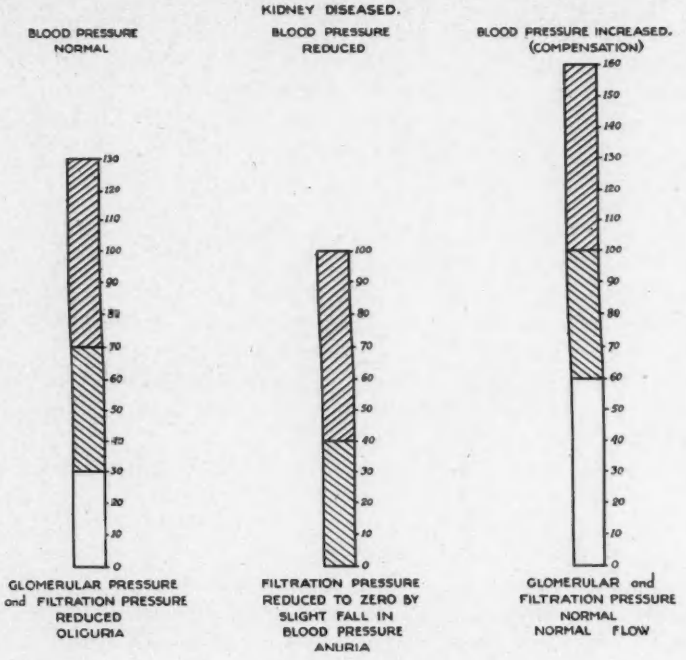

KIDNEY DISEASED.
BLOOD PRESSURE NORMAL
BLOOD PRESSURE REDUCED
BLOOD PRESSURE INCREASED. (COMPENSATION)
GLOMERULAR PRESSURE and FILTRATION PRESSURE REDUCED OLIGURIA
FILTRATION PRESSURE REDUCED TO ZERO BY SLIGHT FALL IN BLOOD PRESSURE ANURIA
GLOMERULAR and FILTRATION PRESSURE NORMAL NORMAL FLOW

Fig. 5

There is no doubt that the kidney is stimulated into greater activity by the presence of waste products in the blood. The diuresis, and the increased concentration of urea in the urine, after administration of this substance by the mouth, is an example of this form of stimulation. It, however, is not comparable to the hormonic stimulation of the pancreas. This gland secretes its own special ferments, et cetera, when stimulated chemically by the hormones.

The kidney only eliminates waste products already present in the blood, and in proportion to their amount in the circulation.

There is no evidence that the renal excretion is under the influence of any nervous or hormonal mechanism. Indeed there is no necessity for such a mechanism. The digestive glands, and for that matter all glands of external seecretion, act intermittently. A comparatively short period of intense activity is followed by a long period of rest. They must have some nervous or chemical impulse to call them into activity at the appointed time, otherwise the whole mechanism of the body is thrown out of gear. The kidney acts continuously, and its action is controlled by (1) the amount of blood passing through it, and (2) by the amount of waste material in the blood. The first of these conditions depends on the general blood pressure, and on the action of the vasomotor nerves of the kidney itself. It is obvious that a complete stoppage of the renal circulation gives rise to anuria, with a rapid destruction of the entire organ, but it is also possible to produce an anuria by diminishing the blood pressure without apparently jeopardizing the renal epithelium.

I have already stated that the filtration pressure in the glomeruli is about 60 mm. of Hg. Excretion ceases when the pressure in the uriniferous tubules rises to this figure, as then the available filtration pressure is balanced by that in the glomerular space. Filtration is impossible when the pressure on both sides of the filter membrane is the same. This is the mechanical effect of a purely obstructive anuria. On the other hand, any fall of the general blood pressure is accompanied by a corresponding fall of the filtration pressure in an unobstructed kidney. In this case, the difference between the pressure in the aorta and that in the glomerular vessels is unchanged, assuming there is no compensatory vasodilation. It remains about 30 mm. of Hg. The osmotic pressure of the plasma colloids is also unchanged. Therefore any reduction in the aortic pressure is accompanied by a corresponding fall in the filtration pressure. It follows that a fall in the general blood pressure of 60 mm. of Hg. results in anuria, as the glomerular filtration pressure is then reduced to zero. If the fall is less than 60 mm., excretion is diminished. This is the reason why any condition accompanied by severe shock may give rise to anuria. This anuria persists till the blood pressure rises again. Once this happens, the excretion

rapidly returns to normal, thus showing that the renal epithelium has not suffered. Anuria from shock may last for as long as three days, and terminate in complete recovery.

Up to this I have considered only normal kidneys. Any surgical disease, with the possible exception of new growths, is accompanied by changes in the renal circulation. Such changes are observed in uninfected kidneys, but are usually more marked when infection is present. They are found in hydronephrosis, in aseptic lithiasis accompanied by dilatation of the calices, in pyelonephritis, and are extremely marked in cases of nephritis. In hydronephrosis the veins are first involved, but changes in the arterioles are soon observed. In any renal infection that has persisted for some time arterial changes are also demonstrable. The narrowing of the arterioles in chronic tubulonephritis is so well known that it requires no further mention.

The effect of these vascular changes is to increase the difference between the aortic and the glomerular blood pressure. As long as the general blood pressure remains constant, these arterial changes in the kidney simply reduce the filtration pressure, and the only means of compensating for this reduction is to increase the aortic pressure. One is inclined to wonder if the general hyperpiesis so often observed in arteriosclerosis of the kidney is not an attempt to compensate for the diminished filtration pressure in the glomeruli. The net result of these arterial changes in the kidney is that anuria can be produced by a smaller fall in the general blood pressure than in the case of a normal organ.

It is possible, therefore, to explain complete anuria following obstruction of one kidney on the assumption that it is a result of a fall in the general blood pressure, and that a comparatively slight fall is sufficient when the unobstructed organ is diseased, but a much larger fall is necessary if it is healthy. This is an alternative to the theory of "reflex anuria," and it is the only alternative I can suggest. One must next consider which of these rival theories fits in best with facts as we now know them.

There is no doubt that the excretion of urine can be influenced in a reflex manner. The application of cold to the skin of an animal is accompanied by a diminution of excretion. This has been shown to be due to vasoconstriction of the renal vessels, as, although the general blood pressure rises, the size of the kidney diminishes.

Stimuli arising from the lower urinary tract, such as irritating urethral injections, act, I believe, in a similar manner. On the other hand, a mild stimulus may produce vasodilation. A partial obstruction of the ureter in animals may give rise to increased secretion from the corresponding kidney. A non-obstructing ureteric calculus in man often causes a similar unilateral diuresis. In both cases, the urine resembles that obtained by stimulating the vasodilators of the kidney, in that it is more copious, contains more chlorides, and is less acid than normally.[4]

The question of a crossed reflex is more difficult. It has been invoked to explain these puzzling cases of calculous anuria. The first experimental work I know of was carried out by Cohnheim and Roy.[3] They stimulated the peripheral end of one splanchnic, and obtained an elevation of the blood pressure to over 200 mm., a reduction of from 15 to 18 per cent in the volume of the kidney on the same side, and complete anuria. Fahr[7] has shown that the cessation of excretion on the opposite side was not due to reflex action, as it occurred only when a considerable number of the splanchnic fibers crossed the opposite kidney. In this condition, stimulation of one splanchnic would act *directly* on both kidneys.

The supporters of the reflex theory lay much weight on the experiments of Gotzl[10] and Koenneke.[14] The former produced anuria in the opposite kidney by tying one ureter. His experiment, was successful, however, in only three out of twelve cases, and the maximum duration of the anuria was sixty-five minutes. Koenneke inserted catheters into the ureters, so that the transitory anuria he obtained may have been due to swelling of the mucous membrane, and not to reflex inhibition. In any case the anuria lasted for only half an hour. No one has produced experimentally the long continued anuria observed clinically, except when it was due to a marked fall in blood pressure, as for example after division of the splanchnics, or section of the spinal cord.

Experiments in the opposite sense have been more conclusive. Gmelin[8] failed to produce reflex anuria, or even any alteration in the rate of flow from the opposite kidney, when its fellow was stimulated in every possible manner. Caulk ligated one ureter in more than 100 dogs, and stated that "there was not a single case of suppression of urine except for a temporary cessation of function." Other investigators have obtained similar results.

The result of experimental investigations show that (1) urinary excretion is not controlled by a nervous mechanism, and that the kidneys can function normally after complete division of the renal nerves, (2) that it is not possible to produce reflex inhibition of one kidney by stimulating its fellow, except a passing action due to vasoconstriction, and (3) that urinary excretion can be inhibited by a marked fall of the general blood pressure.

If we turn to the cases of so-called "reflex anuria" observed in man, we find that they have one point in common. That is that the anuria is always associated with a fall in blood pressure. Unfortunately the sphygmomanometer readings are rarely given in the case reports, but one can infer that they are low from the description of the patient's condition. An acute renal colic is always associated with a marked fall in blood pressure, due to the pain and vomiting. In the cases where anuria followed nephrectomy, shock was severe, and the blood pressure could not rise again owing to pain from pressure of a drainage tube (Israel), or to the presence of clamps left on the pedicle (Rovsing[13]). In the case reported by Nicholich,[16] the operation was difficult and prolonged, and was followed by severe shock. In these cases, which are frequently quoted as examples of reflex anuria, there must have been a profound fall in blood pressure, and I contend that this alone was the cause of the anuria.

In cases of calculous anuria, where the unobstructed kidney was supposed to have been healthy, pain is always severe. In that reported by Neuwirth,[17] it was unaffected by morphia, but was relieved by an injection of novocain round the semilunar ganglia. This was followed by a copious excretion of urine from both kidneys. In the few cases of unilateral obstruction with anuria which I have seen, the pain was intense, and the pulse hardly perceptible. Pain was also severe in cases collected from the literature.

Severe pain is always associated with a fall in blood pressure, which rises again only when the pain is relieved by sedatives, or by local anesthetics. The longer it lasts, the more difficult it is for the patient to recover. The effects of a fall of blood pressure are cumulative. The cardiac output is diminished owing to deficient circulation in the heart muscle. The tissues generally are insufficiently oxygenated for the same reason. This causes the osmotic pressure of the tissue fluids to rise, with the result that fluid is abstracted from the blood vessels. Thus a vicious circle is created, which must

be broken before the patient can be resuscitated. The first step is to relieve the pain, the second is to stimulate the heart. The kidneys do not require stimulation; their failure is secondary only to the circulatory disturbance, and they are capable of functioning as soon as the circulation through them is adequate. In this way anuria following traumatic shock, or acute intraperitoneal disturbances, such as perforation of a gastric ulcer, can be explained. It is simply a prerenal anuria due to deficient circulation.

Total anuria following obstruction of one kidney may also be explained in a similar manner. In these cases the pain arises from the obstructed organ. If it can be relieved by displacing the calculus, or by blocking the nerves, the blood pressure will rise, and excretion becomes re-established. In these cases we have a postrenal anuria of the obstructed kidney, coupled with a prerenal anuria of its fellow. When the unobstructed kidney is diseased, the filtration pressure is low compared with the general blood pressure. A slighter fall will therefore put it out of action. This means that the painful stimulus is less intense, and in some cases it may be only slight. In fact the amount of pain necessary to produce complete anuria is a rough measure of the efficiency of the unobstructed kidney. A badly damaged organ ceases to function when the constitutional disturbances are comparatively slight, while it requires extreme pain and profound collapse to put a healthy kidney out of action.

In a few instances the unobstructed organ has been exposed by operation. It was usually described as being enlarged and hyperemic. This appearance at first sight may lead to the conclusion that the circulation through it was unimpaired. This, however, is not the case. The blood pressure falls because the patient bleeds into his "splanchnic lake." The abdominal organs are able to contain practically all the blood in the body, when their blood vessels are dilated owing to inhibition of their vasoconstrictors. In cases of shock there is a marked contrast between the engorgement of the abdominal viscera and the anemia of other parts of the body. Now, the kidneys form a part of the splanchnic area, and, although they may be filled with blood, this blood is under low pressure, and is really stagnant. Engorgement, therefore, is a sign of circulatory failure.

These circulatory changes may also be used to explain why the

obstructed kidney is occasionally found to be empty. In most cases, the renal pelvis is distended, but occasionally it contains no urine. This has been observed both when the organ was exposed during operation, and in cases where a ureteric catheter was passed above the calculus. Drainage beside the stone might occur during the manipulations necessary to free the kidney from its bed, but if urine escaped beside the catheter its appearance would be noticed through the cystoscope. I think it safer to presume that in some cases the renal pelvis was really empty. Certain authors have assumed that this condition was due to a unilateral inhibitory reflex from the ureter to the kidney above it. The existence of such a reflex is extremely problematic. A simpler explanation is that the kidney, which is already more or less fibrotic through the action of the stone, is unable to secrete owing to a comparatively moderate fall in blood pressure. It is not an absolutely healthy organ, and has a low filtration pressure. A comparatively slight degree of circulatory failure is thus sufficient to put it out of action. The anuria in such cases is prerenal.

My opinion is that the phenomena observed in cases of calculous anuria can be explained in a perfectly satisfactory manner if one takes account of the general and local disturbances of the blood circulation, and that it is unnecessary to invoke the unproven theory that they are due to reflex inhibition.

TERMINAL ANURIA

I have already mentioned that the anuria associated with lithiasis is not always obstructive. To use Legueu's nomenclature, we have anuria caused by stone, and anuria accompanied by stone. In the latter case the anuria is usually terminal, and is ascribed to renal failure. It is exactly similar to the terminal anuria of chronic pyelonephritis, and similar conditions. In these cases one usually finds a prolonged febrile period, during which, although a fair quantity of urine is eliminated, the blood urea slowly rises, and the usual signs of uremia appear. This is followed by a short period, usually two to three days, in which the temperature suddenly drops to subnormal, and suppression supervenes. The only point I would like to raise is that the suppression is usually put down to renal failure, but in all the cases I have seen it was preceded by a marked fall in blood pressure. I believe that the suppression is really due to

heart failure, and that the treatment should be directed towards re-establishing the circulation. At present, one attempts to stimulate the kidneys, and this line of treatment always fails. I believe that this form of anuria is due to circulatory failure, and is therefore prerenal. This, however, is a more or less academic distinction, as the outlook is usually hopeless. I mention it only because it brings this form of anuria into line with those already discussed.

REFERENCES

1. Carrel and Guthrie: Science. 23:394, 1906.
2. Caulk: Post-renal Anuria. Jour. Urol., 13:265, 1925.
3. Cohnheim and Roy: Virchow's Arch. f. path. Anat., 92:424, 1883.
4. Cushney: The Secretion of the Urine. 1917, p. 12.
5. Eliot: Etiologie, Pathologie et Traitement de l'Anurie au Cours de la Lithiase et des Tumeurs et Néoplasms pelviens. Thèse de Paris, 1910.
6. Engel: Quoted by Gruber, loc. cit.
7. Fahr: Ueber die morphologischen Grundlagen der Anurie. Verhandlungen der deutschen Gesellschaft für Urologie. VII Kongress, 1926, p. 218.
8. Gmelin: Tierexperimenteller Beitrag zur Frage der reflectorischen Anurie. Zeitschr. f. urol. Chir., 21:182, 1926.
9. Gottstein: Nephrolithiasis. Handbuch der Urologie. Lichtenberg, Voleckker and Wildbolz, 4:494.
10. Gotzl: Untersuchungen ueber reflectorische Anurie. Pflüger's Arch. f. d. ges. Physiol., 83:128, 1901.
11. Gruber: Entwicklungsstörungen der Nieren und Harnleiter. Handbuch der speziellen pathologischen Anatomie und Histologie. Henke and Lubarsch, Part I, 6:66.
12. Guizette and Pariset: Quoted by Gruber, loc. cit.
13. Israel, J. and W.: Chirurgie der Niere and des Harnleiters, 1925, p. 332.
14. Koenneke: Zeitschr. f. urol. Chir., 13: Nos. 3 and 4.
15. Legueu: La Lithiase rénale, Encyclopédie française d'Urologie, Vol. II, 1914.
16. Nicolich: Anurie réflexe après Néphrectomie pour Pyonéphrose; Décapsulation de l'autre Rein; Guérison. Jour. d'Urol., 20:41, 1925.
17. Neuwirth: Ein Beitrag zur Therapie der Reflexanurie. Zeitschr. f. urol. Chir., 11: Nos. 3 and 4.
18. Quinby: The function of the kidney when deprived of its nerves. Jour. Exper. Med., 23:535, 1916.
19. Rubritius: Die Klinik und Therapie der Anurie. Verhandlungen der deutschen Gesellschaft für Urologie. VII Kongress, 1926, p. 233.

DISCUSSION

DR. VINCENT J. O'CONOR (Chicago, Ill.): I would like to present an interesting problem of anuria associated with calculus disease which I have had recently. A woman fifty-four years of age, who had passed gravel at the age of eighteen with no subsequent symptoms, began to have frequency and urgency of urination last December. She went to a clinic where she was examined and it was found that she had a complete reduplication of the ureter and pelves on the right side, the upper pelvis being completely filled with stone and the lower end of the ureter from this pelvis containing a very large stone. The lower half of this right double kidney showed a hydronephrosis with a capacity of about 6 ounces but no stone. The left kidney had a single ureter but the x-ray showed a complete stone cast of the upper, middle and lower calices. (Slides)

Following this study the patient was advised to have surgery and consulted me among others. At the time that I first saw her she had a blood pressure of 120/80, normal blood chemistry, very purulent highly infected colon bacillus urine. We discussed the question of surgery and she went home to decide as to operation.

A month later I was called to the hospital to see her. She had passed only a cupful of urine in two days. She was not acutely ill, blood pressure 110/80, and had no pain or colic whatsoever. Her tongue was dry and she was slightly drowsy. Blood urea nitrogen was 50 mgm. and creatinin 4 mgm.

I made a cystoscopic examination for the first time and found that she had a ureterocele of the meatus coming from the upper half of the right kidney. I was able, however, to catheterize both ureters on the right side and put a third catheter into the left kidney pelvis. Following catheterization I withdrew from the lower half of the right kidney 3 ounces of clear, uninfected urine and a teaspoonful of thick urine from the upper half. On the left side I obtained no drainage. These catheters were left in place twenty-four hours; she was given the usual supportive treatment—Ringer's solution and glucose intravenously, et cetera, but there was no drainage from any of the catheters and catheterization of the bladder drew forth a tablespoonful of debris only. Creatinin at

the end of seventy-two hours after the onset of anuria was 7.5 mgms. per 100 c.c. I was rather at a loss to figure out just which obstructive condition in the three ureters might be the underlying cause of the anuria, and since I could pass a catheter to each of the three renal pelves I wondered if operation would bring about a return of urinary excretion.

Under ethylene I made a Gibson incision, and removed the enormous stone from the enlarged ureter which drained the upper half of the right kidney. I then did a nephrotomy of the upper half of the kidney, removing a complete stone cast of the pelves and calices, and closed the nephrotomy wound with Lowsley's ribbon gut sutures. I made a nephrotomy opening of the hydronephrotic lower half of the right kidney.

The patient stood the operation very well and in the first twelve hours passed 3 ounces of urine from the hydronephrotic kidney and 4 ounces from the upper half. The next twelve hours she drained 8 ounces from the two catheters in the right kidney, 4 ounces from the bladder. After this time she promptly began to excrete by the tenth day from 1800 to 2000 c.c. of urine daily. She made an uneventful convalescence and left the hospital three weeks after operation with both nephrotomy tubes removed and normal blood chemistry, including a normal creatinin.

It is difficult for me to understand the underlying cause of the onset of the anuria in this patient, since she had had no instrumentation or cystoscopic examination for a period of two months, and had undoubtedly had the same general health which she enjoyed the first time I saw her and had had for a number of years.

DR. LEON HERMAN (Philadelphia, Pa.): I would like to report a case that may throw some light on the question of reflex anuria which I think should prove of some interest to Mr. Swift Joly. The patient, a boy aged nine, was seized with acute transverse myelitis of the lower cervical cord. He was the son of a doctor and a great many doctors in Philadelphia were interested in him. It was decided not to operate on him, and he developed the usual retention. Catheterization was employed, and following this he developed a peri-urethral abscess and it was necessary to do a suprapubic drainage, after which he developed multiple stones in the bladder. He then developed stones in the kidneys and because of an infected right kidney with stones, I did a nephrolithotomy. He

went along for a time passing many stones from the bladder and kidney and then one day developed anuria.

There was total paralysis and anesthesia below the nipple line, so that pain was not a factor. I made a cystoscopic examination through the suprapubic wound, passed a catheter in the left ureter, met an obstruction a few centimeters below the kidney, prepared stereoscopic plates and found an obstructive stone. In the meantime the right kidney stopped secreting. He wasn't secreting a drop of urine by way of the suprapubic wound or the nephrotomy wound on his right side.

It was decided to cut down on the left kidney and remove the ureteral stone, which was associated with many in the left kidney. Following operation, the left kidney started to work, secreted copiously at once, but the right kidney failed to function for about seventy-two hours. Thereafter it immediately started in to secrete again. So this boy had suffered what we looked upon as a true reflex anuria in a kidney that was wearing a nephrotomy tube. In this case pain was not a factor in reflex anuria.

Dr. Frank Hinman (San Francisco, Calif.): I am sure we all enjoyed very much Professor Joly's presentation. The explanation of anuria which has been given is new and original. The explanation of anuria in obstruction with which we are familiar is that it is either one of retention, as where there is complete obstruction, or of cessation of secretion as in the reflex type, where there is spasm of the blood vessels and an anuria of secretory type. In experimental work in animals, it is a fact that there are two very distinct pathologic changes with complete obstruction of the ureter. In one there is an anuria at the onset and a pathologic change which is one of primary atrophy. In the other, where there is not an anuria, the development of hydronephrotic atrophy occurs. Hydronephrosis cannot develop with anuria. Therefore, in cases with complete obstruction of the ureter and the development of hydronephrotic atrophy, there is not an anuria but a retention.

An interesting type of anuria from obstruction in the tubules occurs in hemoglobinuria. The hemoglobin crystals precipitated in the blood or in the tubules after the urine is secreted block the tubules and produce obstruction with anuria. The recognized treatment in these cases is to give large doses of alkali, which dissolves these hemoglobin crystals and re-establishes a urinary secretion.

I will enjoy reading Dr. Joly's paper when published and express my appreciation in having heard it.

DR. CHARLES M. MCKENNA (Chicago, Illinois): My purpose in arising is to get information rather than to give it. I would like to ask Professor Joly if he will tell us what experience he has had with lipomatosis following the removal of kidney stone, especially with bilateral stone. By that I mean the fat replacement in or about the kidney. We have had several cases where this had occurred in unilateral cases. To me it would be difficult to know when to operate and when not to operate.

DR. F. R. HAGNER (Washington, D. C.): I have seen any number of patients who have had almost a complete anuria, or complete anuria, with high blood chemistry. It has been my experience that a sudden rapid secretion of urine is a most unfavorable symptom. You will be greeted by the nurse telling you that the patient is much better, that he has passed a large amount of urine, yet that patient is usually dead in twenty-four hours. Of course, this urine is of low specific gravity. I have hardly ever seen one of these patients that did not die promptly following the rapid secretion of urine.

DR. JOSEPH HUME (New Orleans, La.): I wish to say a word of appreciation of Professor Joly's paper and to bring up certain types of anuria that are worth while thinking about. The first is the type that Dr. Hinman described as hemoglobinuria. In the South, I have seen a number of cases of complete anuria for many days from black water fever, where the tubules have been stopped up by hemoglobin. In those cases you have to force with water, give alkalis and they do respond to decapsulation.

The second group is a group to which Fenwick originally called attention, where you have a bleeding kidney and where upon cystoscopy the bleeding stops instantaneously. I have seen the efflux bloody and by the time a catheter is passed up into the kidney the efflux is clear, and yet the kidney goes on secreting. That is a peculiar thing.

The third peculiar case I saw was that of a nurse who reported she hadn't voided for forty-eight hours, a young, healthy woman. We could find nothing the matter with her. I kept her under close observation for twenty-four hours more; that was seventy-two hours. I then made a cystoscopic examination, going up both ure-

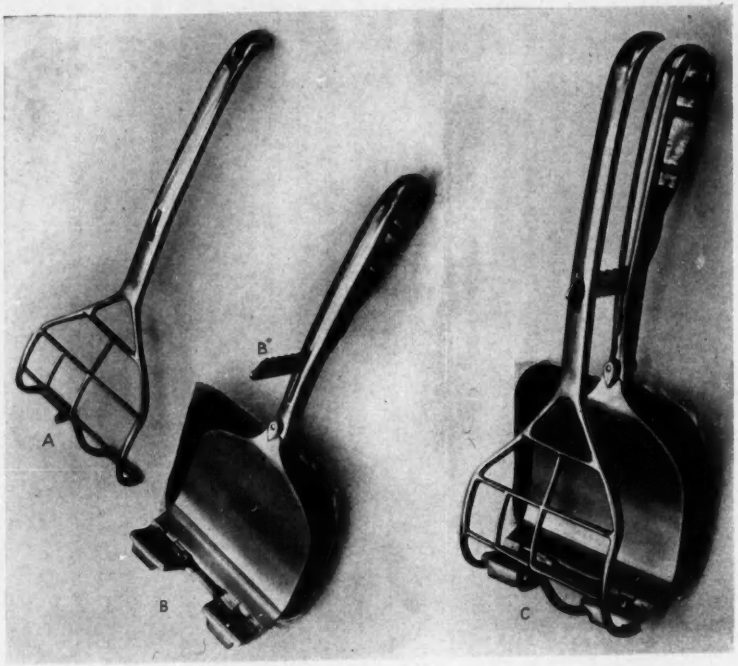


Fig. 1. *A* and *B*, Gridiron retractor separated. *C*, Gridiron retractor assembled.

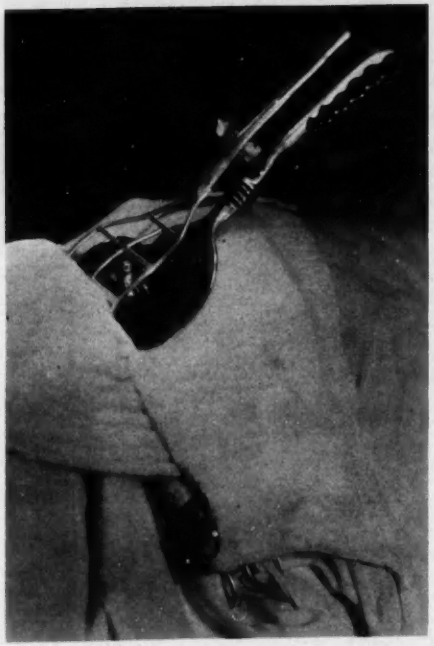


Fig. 2. Kidney held by gridiron retractor for making x-ray.

ters. There was no retention, no trouble, and I washed those kidneys out with normal salt solution and kept the catheters in for six hours and didn't get a bit of urine. I then remembered a suggestion of Professor Henry Morris and gave a half grain of morphine. This patient had a body weight of about 110 or 115 pounds. Within three-quarters of an hour, she started to secrete copiously and I watched over her for three years and nothing ever developed.

The final case happened at Christmas, and this is a case in which it is difficult to get around the reflex theory. A competent surgeon telephoned me over long distance. He had taken out a kidney, for stone, of a man of twenty-eight who was perfectly healthy. There was no shock and no disturbance. The man for five days had voided only 3 or 4 ounces of urine, almost complete anuria. He had been given diuretics, he had been given intravenous glucose on two separate days, and the remaining kidney was catheterized, yet nothing was found. The question was what to do, what caused the condition. Of course, I thought of a decapsulation but first thought those cells for some reason were not stimulated and advised giving him an injection of salyrgan; this was done, and in six hours I received the telephoned message that the patient was voiding copiously. He was reëxamined when he was on his feet and nothing could be found to account for the case of anuria.

Dr. Arthur B. Cecil (Los Angeles, Calif.): I thought it might be of interest to show an instrument that I devised for taking x-ray pictures upon exposure of the kidney for the localization and fixation of renal stones. The instrument consists of an anterior (Fig. 1*A*) and posterior blade (Fig. 1*B*). The posterior blade (Fig. 1*B*) carries an x-ray film which has been wrapped in sterilized cellophane. Cellophane has been used because it is very thin and because it permits of sterilization by boiling. The anterior blade is made in the form of a gridiron, the openings in the upper pole of which are somewhat different than those in the lower pole. On exposing the kidney the blade (Fig. 1*B*), carrying the x-ray film wrapped in cellophane and fastened down by an overlying plate of aluminum marked *B′* is immediately placed beneath the kidney before the kidney is in any way opened. The gridiron blade (Fig. 1*A*) is now hinged onto the blade (Fig. 1*B*) and held in place by the ratchet *B″*. After making the x-ray, the retractor is kept in place, the film is removed with a Kelly clamp and developed.

I believe this instrument will be extremely useful in operating on stone in the kidney. I have recently made some changes in the instrument in that the blade *B″* is also a gridiron blade and the aluminum plate *B′*, which is used to hold the film in place, can be removed so that, having localized stones, one then has the opportunity to be able to palpate through and through the gridiron retractor.

DR. GEORGE R. LIVERMORE (Memphis, Tenn.): Some years ago, I reported a case of pigment in the glomeruli and uriniferous tubules, and, upon looking up the literature, I found that Havill, Lichty and Whipple had found that where dogs had been given large amounts of hemoglobin intravenously it blocked the tubules with hemoglobin. Dogs that they had injected were capable of standing large doses of bichloride of mercury poisoning without very much damage to the kidney. They stood very much more mercury than a normal dog could stand.

Working on this hypothesis, I thought perhaps if we would give the hemoglobin intravenously to persons who had been subjected to bichloride of mercury poisoning, perhaps we might prevent damage to the kidney. I experimented in conjunction with W. R. Amberson and Dr. R. A. Bliss, Jr., at the University of Tennessee, and injected dogs with hemoglobin after they had been given bichloride of mercury poisoning, within an hour to an hour and a half, which would represent the time that the average physician perhaps would be able to see a patient. Unfortunately, all our dogs died and it didn't work out as we had hoped.

Now I think some word of appreciation should be voiced in the work that Dr. Albright has brought before us. (We have already expressed our deep appreciation to Mr. Joly for his contribution.) But such work as Dr. Albright has done is certainly epochal and I think we really should compliment him very much upon it. Recently we (Livermore, Bliss and Prather) did a few experiments to confirm the findings of a diet deficient in Vitamins A and D, and we found that all of our calculi were phosphatic and the urines either alkaline or neutral. There was also great damage to the mucous membrane of the urinary tract with exfoliation of the epithelium and marked swelling, and hence we figured that perhaps there might be some obstructive feature added to the metabolic changes. We also concluded that perhaps the deficiency in one, I mean the failure of one metabolic process, might result in deficiency

of another. I think Dr. Albright's experiments prove this very conclusively.

Dr. Alexander Randall (Philadelphia, Pa.): I think this meeting ought not to pass without thanking Dr. Albright for his brilliant work and also Dr. Barney for his very clear thoughts in his paper on the phase of parathyroid pathology in stone formation. This adds another to our already rather full group of presumptive theories for stone formation.

Mr. Joly has brought out, of course, his most interesting colloidal chemical story. We are also familiar with the story of stasis, the story of vitamin deficiency and the story of infection, but one can not help asking the question: If these theories, if I may so term them, presumptive theories of actual causes of stone, are correct, where do they fit into the man who is a constant phosphorturic or a man who is a constant cystinuric?

It is nice to see our association getting further into the answer of this age-old problem. Yet I cannot help feeling that each one of these theories only fills a niche in the chemistry of stone formation, and are themselves but secondary factors in the actual cause of stone. Dr. Albright tells us 10 per cent might be parathyroid lesions. There must be back of each one of these presumptive theories an actual pathologic factor which is the primary cause and which in each case, because of other disturbed pathology or disturbed metabolism, makes a patient form a stone. I am of the opinion that this primary cause is an ulceration of the renal papillæ. We have been trying to get at that factor and were trying to create artificial aseptic lesions of the renal pelvis. If we could by such means create a focus on which crystallization may occur and on which, when it occurs, there is also a time element that would allow a stone to grow, we would be in a position to vary these secondary factors. There is a time element there that has to have time to work, because undoubtedly a lot of men are constantly putting out showers of crystals, but there has to be something else which allows that disturbed crystallization to localize and be given time to grow a stone. I thought for a time that our experiments were getting near to an answer. In fact, we had experimental dogs that showed shadows in their renal region. It seemed so perfect that we said, "We will sacrifice these animals and see what the answer is." We did sacrifice them. They had no stone and when we

went back to our plates, we realized that we were looking at shadows which arose from pigmentation of the nipple.

It just brings back to us that "life is short and art is long," but research seems to be much longer, and in this one problem of stone, research certainly is ages old.

DR. CHARLES C. HIGGINS (Cleveland, Ohio): As Dr. Barney stated, there are certain clinical observations that lead us to infer that there is a definite relationship between stone formation and the absence of certain essentials in the diet. We know that stone areas (or regions in which calculi are usually prevalent) occur in India, China, the valley of the Volga in Russia, and Germany; Mr. Joly states that they also occur in Westmoreland and Derbyshire in England. According to the reports of Holmes and Coplan the stone areas in the United States are in Southern Florida and in Southern California.

It is also being observed clinically that there has been a decrease in the instance of calculous disease in children where there has been improvement in dietary conditions. Mr. Joly in his recent book stated that calculous disease is no longer one of infancy or childhood in England, but rather one of adult life, yet in the valley of the Volga in Russia 60 per cent of cases of lithiasis occur in children under fifteen years of age.

Finally, there also is definite evidence that calculi may be produced in persons taking a deficient diet. Dr. Vincent O'Conor has also reported a series of patients in whom renal calculi developed when they have been on the Sippy diet with high alkaline medication for a long period of time.

In our work in the experimental production of stones in rats by Vitamin A deficient diets, three constant findings are observed. The first is infection, the second is persistent alkalinuria, and the third is keratinization or metaplasia of the epithelium of the renal pelvis, ureter and bladder. I am positive that infection in this experimental work is not the sole factor in the production of stones. In the first place, the incidence of infection does not keep pace with the instance of stone formation in the early stages of the experiments. If ammonium chloride is added to the diet, tending to acidify the urine, it is more difficult to produce calculi. It is very true that, as Dr. Deaver stated years ago, a dog is a dog and a man is a

man, and what we find in the laboratory may not always be substantiated by clinical observations.

Recently, however, Dr. Wolbach and Dr. Blackfan, and Dr. Mori have reported cases of children who died of some intercurrent disease after they had been taking a diet deficient in Vitamin A for a long time. In these cases at autopsy they observed metaplasia of the epithelium of the genito-urinary tract and in the majority of cases the urine was alkaline.

The chemical factors involved in the experimental production of stones may now be satisfactorily explained to satisfy the requirements stressed by colloidal chemists and it is undoubtedly true that the high alkaline urine associated with keratinization of the epithelium are the important factors. I am positive that vitamin deficiency disease is not the cause of all calculi, as one also finds calculi associated with metabolic disease. There are also a group of cases associated with hyperparathyroidism. Experimentally, calculosis can be produced in the parenchyma of the kidney by injection of parathormone, but it has not been possible to produce stones in the pelvis of the kidney or bladder stones. It is only by careful interpretation and analysis of all the experimental work and correlation with all clinical observations that, as Dr. Randall stated, it may finally be possible to find perhaps a single etiologic factor associated with all calculous disease.

Dr. J. Dellinger Barney (Boston, Mass.): I rise in the first place to say that I would like to do that which I cannot, namely, discuss Mr. Joly's paper. All I can do is to express my intense admiration for the masterly way in which he has presented it.

In the second place, partly due to modesty, but largely due to lack of time, Dr. Albright was entirely unable to give you the long and complicated story of the biochemistry and physiology of parathyroid disease into which he has gone very deeply and about which you will hear more. We feel sure that it is a great factor in the production of a certain percentage of stones, and research along the line which he is doing in parathyroid disease may lead to the discovery of the etiology of stones of other types.

Of course, all this investigation is open to a good many new avenues of thought and approach. We know little as to why stones are seen in cases of fracture. Professor von Lichtenberg, at our meeting in Manchester, Vermont, some years ago, in discussing a

case which I reported, remarked that stones in fractures were not uncommon, at least in his country. My case was that of a boy with a fractured femur who developed bilateral stones while he was in the hospital. He eventually dissolved or broke up those stones and passed them out, so he left the hospital with kidneys free from stones. I confess we don't see many stones in fractures in our hospital.

Then there was some evidence that long continued recumbent posture has something to do with stones. I just mention these things because they have come to our attention during our thought on the subject. I also want to call attention to the stones found in lymphoblastoma, uric acid stones deposited in the tubules of the kidney. Dr. O'Conor has called our attention, in the discussion of Dr. Randall's paper some time ago, to the influence of the Sippy diet and that has also been noted by Dr. Albright.

I would like to mention a boy whom I saw eighteen years ago, a boy of seven. At the age of three he began to pass stones. His mother brought in a quart preserve jar full of stones the child had passed. He came to me because a stone had been caught in his urethra and he couldn't pass it. Those stones were pure calcium oxalate. They were examined by Professor Folin at the Harvard Medical School. The x-ray showed both kidneys filled with stones, so they looked like pyelograms—separate stones and stones impacted in the lower ureter. Professor Folin told me to omit all milk and milk products, both raw and cooked, and that was done. The boy passed out most of the stones he had had as shown by x-ray three or four months later. He kept on with that diet, and at another time three or four months after that, showed himself to be almost entirely free from stones. Shortly afterward, unfortunately, he developed pneumonia and died. No autopsy was obtained.

I don't know the answer. I just mention it as a very puzzling and interesting case of some metabolic error, not uric acid.

All these investigation of Dr. Albright's, it seems to me, show that in all cases of stone it would be very desirable to do a routine calcium and phosphorus estimation as well as a pretty thorough examination by x-ray of the bones. It may throw light on the case and it may prove to be a case of parathyroid disease.

MR. J. SWIFT JOLY (London, England): It has really been a great privilege to come here and listen to this discussion on para-

thyroid disease in connection with calculus formation, and I assure you I am delighted to have had the opportunity of hearing these extraordinarily valuable papers. I should certainly look forward with keen interest to anything that emanates from the Boston school.

With regard to the questions that were asked me about my paper entitled "Anuria," Dr. Herman mentioned a case of paralysis at the level of the lower cervical region associated with calculus formation in which there was anuria from a nephrostomized kidney. In that case there are two factors: first of all, the blood pressure is already low on account of the spinal condition and, second, the kidney is already damaged. It has been operated on. It has been the site of many calculi and has been affected so that that kidney was working on a very small margin and a very slight change in the blood pressure might be the principal reason to throw it out of action.

One feels dubious about saying that a thing is due to a reflex mechanism when the physiologists are not able to reproduce such a reflex mechanism. I really doubt and I think it impractical to prove that a secretion of urine is under the influence of the nerves, as it must be if one can produce a reflex inhibition, except perhaps by constriction.

I think the same applies to Dr. Hume's interesting case of anuria after operation. I think there must have been some change in the blood pressure because he said that the secretion was reëstablished after the injection of the saline solution. The amount of fluid influx probably was great enough to raise the blood pressure sufficiently to enable the kidney to function again.

URINE FORMATION IN THE AMPHIBIAN KIDNEY

A. N. RICHARDS, Ph.D. (by invitation)

From the Laboratory of Pharmacology, University of Pennsylvania, Philadelphia

Quantitative studies of the composition of glomerular fluid collected from renal corpuscles of frogs and Necturi have provided strong evidence in support of the doctrine that the glomerular process consists essentially in ultrafiltration. These studies have included determinations of total molecular concentration, of electrical conductivity, of pH, of concentrations of chloride, inorganic phosphate, glucose, urea, uric acid, creatinine, and of the injected dyes phenol red, indigocarmine and neutral red. In each of these categories the composition of the glomerular fluid was found to be the same as that of plasma or of a protein-free filtrate from plasma.

The ultramicro-analytic methods which were developed for the study of glomerular fluid have recently been applied to fluid collected from different levels of the uriniferous tubules of these animals, with the result that we are now able to identify more precisely than has hitherto been possible the loci of some of the changes which the glomerular filtrate undergoes in its passage through the tubule. This account is a résumé of results obtained largely by my colleagues during the past two years. The work has been greatly aided by generous financial support from the Commonwealth Fund of New York.

The urine of amphibians is normally a much less concentrated fluid than is the glomerular filtrate. This is owing largely to the fact that it contains very little chloride. This disappears from the glomerular filtrate in passing through the tubules because it is reabsorbed into the blood. Amphibian urine also contains no glucose and very little bicarbonate. The amphibian kidney is eminently suited, therefore, to the study of reabsorptive processes in urine formation. Some of the diffusible constituents of plasma, however, appear in the urine in higher concentration than in plasma. Urea, uric acid, creatinine, inorganic phosphate and some of the dyes are in this group. Study of changes in the concentration of these substances within the tubule should throw new light on the concentrating power of the kidney.

Total Molecular Concentration, Chlorides and pH.—No very significant changes in these are accomplished in the glomerular filtrate during its passage through the proximal tubule. Its reaction remains the same; its total concentration and its chloride concentration are, if anything, slightly increased. Its volume is diminished. Only when the fluid enters the distal tubule does it begin to resemble urine in these respects. Progressive diminution in total concentration of solids and in chlorides occurs so that when it issues into a collecting duct it is strongly hypotonic to blood, contains very little chloride and bicarbonate, and is acid in reaction. The greater part of the change in reaction appears to take place in a short section of the proximal third of the distal tubule. We have no information with which either to describe or explain the process by which the cells of the distal tubule transfer chloride from lumen to blood or by which acidification of the fluid is accomplished. It may be regarded as certain that both changes are the results of specialized activities of the epithelial cells.

Glucose.—The glomerular urine contains the same concentration of glucose as blood plasma; urine as it leaves the kidney contains none. When fluid is collected from the proximal tubule after having traversed about one-quarter of its length, its glucose concentration is found to be only one-half that of plasma. When half its length has been traversed, the glucose concentration is nearly zero. Special experiments in which Ringer's solution containing glucose was passed through the lumen of the distal half of the proximal tubule showed that its cells possess the same capacity to cause glucose to disappear; similar experiments on the distal convoluted tubule show that its cells do not possess this capacity. Hence we are able to say that sugar lost from the blood by glomerular filtration is restored to it by processes which operate in cells of the proximal tubule, not in the cells of the distal tubule.

In amphibians, as in mammals, phlorhizin poisoning causes glycosuria. This is not due to action on the glomerulus, but is the result of abolition of the power of cells of the proximal tubule to transfer glucose from lumen to blood. The glucose concentration of the glomerular filtrate becomes greater as it passes through the phlorhizinized proximal tubule. This change has been shown not to be due to secretion of glucose into the tubule; hence it must be due to reabsorption of water. In Necturi, after phlorhizin, the fluid

which issues from the distal end of the proximal tubule contains on the average 26 per cent more glucose than the blood plasma. This means that about one-fifth of the water of the glomerular filtrate has been reabsorbed from the proximal tubule.

Although the tubule in phlorhizin poisoning loses its active capacity to restore glucose to the blood, it appears still to possess the property of allowing glucose to diffuse back into the blood when the glucose concentration in tubule fluid exceeds that in blood to a certain degree. For if the phlorhizinized tubule be perfused with Ringer's solution containing glucose in concentration 50 to 100 per cent higher than that of plasma, this concentration diminishes. This observation seems to us to be important inasmuch as it reveals a possible flaw in the assumptions of those who have advanced the view that in mammals, as well as in amphibians, the plasma clearance of xylose is equivalent to the total volume of glomerular filtration. This is based on the observation (Homer Smith and colleagues) that the quantitative relations of the excretion of xylose and glucose in phlorhizin poisoning are identical, and that no glucose in phlorhizin poisoning can be reabsorbed from the tubule. If this is true, as the above experiments indicate, that glucose can diffuse out of the phlorhizinized tubule, the unreliability of this means of indirectly measuring glomerular filtration is obvious.

Inorganic Phosphates.—In the urine of both frogs and Necturi, inorganic phosphate is sometimes less and sometimes more concentrated than in blood. In the former case it can be shown that some at least of the reabsorption of phosphates from the glomerular filtrate occurs during passage through the proximal tubule. In the latter case it is shown that only a relatively small fraction of the concentration of phosphates by the kidney is effected within the proximal tubule; only as much as could be accounted for by reabsorption of water. No evidence of secretion of phosphates by the wall of the proximal tubule was obtained.

Urea.—The frog's kidney is capable of excreting urine in which urea concentration is as much as sixty-five times that of the blood. The highest concentration ratio encountered in our experiment is about nineteen; the average, six. In Necturi the concentrating power for urea is much less: highest in our experiments three and five-tenths; average, two. In none of the experiments with Necturus

is there evidence that cells of the tubule secrete urea into the lumen. The concentration in the urine and the total amount excreted can be accounted for by glomerular filtration and reabsorption of water.

In frogs the concentrations of urea, relative to plasma and to urine, encountered in fluid taken from different levels of the tubule are such as to make it hazardous to say that urea has not been secreted by the cells of the tubule; of the final urea concentration attained the fraction which is effected in the proximal tubule is so small that we are led to suspect that if tubular secretion is a factor in urea excretion in frogs, the distal tubule must participate in the process.

Uric Acid.—The concentrations of uric acid in fluid which has passed through the proximal tubule of frogs or Necturi are not higher than can be explained by reabsorption of water. The further concentration accomplished in the distal tubule in frogs (but not in Necturi) is great enough to make decision concerning secretion by distal tubule cells uncertain.

Creatinine.—In Necturus, creatinine is more highly concentrated in the urine than is any other substance studied by us; in frogs the degree of its concentration is very low. The results force us to concede the possibility of secretion of creatinine by the proximal tubule of Necturus, not by that of the frog.

In summary, it may be stated that the two species of amphibians studied are alike in that reabsorption of chloride and acidification of the urine occur in the distal tubule; reabsorption of glucose occurs in the proximal tubule. Active glucose reabsorption is abolished by phlorhizin, but the possibility of passive diffusion of glucose out of the tubule is not. The two species differ with respect to the excretion of urea, uric acid and creatinine. The degrees of concentration and the amounts excreted of urea and uric acid in Necturus and of creatinine in frogs are such as not to require the assumption that these substances are secreted by the cells of the tubules. The possibility is indicated that such an assumption is necessary in connection with the excretion of urea and uric acid in frogs and of creatinine in Necturi. The distal tubules may participate in this process if it exists.

The greater share of the exceedingly difficult labor of collecting

fluid from the renal tubules has been borne by Dr. Arthur M. Walker; the analytic work by Drs. C. L. Hudson, James P. Hendrix and Thomas Findley. Dr. Hugh Montgomery has done the work on pH and Dr. R. T. Kempton has given valuable assistance in identification of the exact points in the tubules from which fluid has been taken.

DISCUSSION

DR. FRANK HINMAN (San Francisco, Calif.): I don't want to make it appear I am qualified to discuss this wonderful presentation. It might be well to emphasize the relationship of the structure of the frog's kidney to the structure of the kidney that we have to deal with clinically. By his earlier work Dr. Richards has proved the modern theories of glomerular function. This more recent study of his seems to prove by his very definite demonstration today many of the theories of tubular function.

The human kidney is homologous in structure to the amphibian kidney with which he has been working. But the problem of secretion by the human kidney or the metanephros is a much more complicated problem than in the amphibian kidney or the mesonephros.

(Slide) This is a drawing of the kidney of Necturus, a mesonephros, which also retains part of the pronephros, which is a distinctly homologous remnant.

(Slide) In the higher forms, such as in reptiles, the development of a loop of Henle begins. The amphibian kidney, as in the snake and the salamander, does not have a loop of Henle. It has an intermediate connecting portion. In the next evolutionary stage, such as the alligator and the lizard and the turtle, there is a beginning, but the first real loop of Henle is in the bird. The kidney of a bird is a metanephros. In some alligators, particularly the crocodile, there is a beginning development of the loop of Henle. The bird is a direct offshoot in the stage of evolution from the reptile. Then in the rabbit you see this enormous loop of Henle.

(Slide) This shows in some of the higher mammals the differences in the length and character of the renal tubule. In man there is a relatively short loop of Henle as compared to the pig, and here in the cat there is sometimes an enormous loop of Henle.

The significance of this with respect to this wonderful work of Dr. Richards in amphibia is the fact that this loop of Henle as a structural change from lower to higher vertebrates cannot be overlooked in the application of his demonstration of the function of the tubule in amphibia to the explanation of the functional activity of the human tubule.

(Slide) One thing to be emphasized is the fact that the human

renal tubule is not a unit. The structural unit in the human kidney is made by the blood supply and there are circles of glomeruli forming cylinders with the blood supply coming up through the center. This blood supply comes from end arteries that go to the glomeruli which have efferent vessels that go to the tubule, but the efferent vessel of a glomerulus does not always go to its own tubule. It goes to the convoluted loops of other tubules in the neighborhood, so that the unit of function in the metanephros is a conglomeration of these tubules, and that explains why in all types of renal insufficiency, the insufficiency is unitary and is not segregated.

RESECTION OF THE KIDNEY

HERMAN L. KRETSCHMER, M.D.
Chicago, Illinois

In view of the fact that the general tendency in the surgical treatment of various lesions of the kidneys has had a distinct trend toward conservatism, and because resection of the kidney is an operation of great possibilities in well selected cases, it does seem strange that the operation has been performed relatively infrequently. In recent publications both Young and Judd call attention to the fact that the operation is rarely performed.

With the development of modern urology and with the many problems calling for solution, particularly from the diagnostic standpoint, it is not surprising that this conservative procedure should temporarily be lost sight of.

Küster, in his monograph published in 1896, collected but thirty cases that had been subjected to a resection of the kidney with a mortality of 16.6 per cent. Perhaps resection fell into temporary disrepute because of the poor results obtained when the operation was first performed. Moreover, during the inceptive period of kidney resection the operation was unwisely invoked, a matter clearly evidenced by the statistics of Küster: in sixteen out of the thirty cases resections were either for tumor or tuberculosis. The lack of refinements of diagnosis in the early cases must be held responsible for some of the failures recorded, since the operation was carried out in lesions which we now know are wholly unsuited for resection, among these lesions being malignant tumors and tuberculosis, conditions requiring a radical operation and not a conservative one.

Resections of portions of normally formed kidneys have been done for various pathologic conditions and many of them were carried out long before the advent of modern urologic diagnosis. Among the various lesions for which resections were done may be mentioned:

Spiegelberg (1870).—Accidentally resected an echinococcus cyst of the right kidney.

Wells (1884).—About one-third of the left kidney accidentally removed in shelling out a tumor in the region of the kidney.

Czerny (1887).—Resected a tumor—angiosarcoma of the kidney.

Keetley (1890).—Removal by lumbar incision of the loose and crushed-off lower extremity of the left kidney after a wagon accident.

Waitz (1891).—Resection for pyonephrosis.

Bardenheuer (1891).—Resection of two cases: one for calculus pyonephrosis, the other for injury.

Kummell (1893).—Reported three cases of resection. The first was a localized inflammatory process, a hard nodule the size of a walnut. The second was an abscess caused by a calculus. The third was echinococcus disease.

Block (1896).—Tumor of the kidney—adenoma.

Moynihan (1902).—Reported three resections: 1. Solitary cyst. 2. Solitary cyst in connecting band of a horseshoe kidney. 3. Tumor.

Rathbun in a recent publication reported a series of six resections.

Resections of double kidneys have been performed more frequently than have resections of normally formed kidneys, but this is undoubtedly due to modern urologic diagnosis. The lesions are generally infected hydronephrosis with or without stone. In this connection it might be well to mention the case of Eisendrath, Phifer and Culver, in which the lesion was bilateral and resection on each side was carried out.

In a discussion of resection of the kidney it is necessary to differentiate between two types: (1) resection of a part of a normally-formed kidney; (2) resection of one-half of a double kidney.

In this series ten resections were done upon ten normally formed kidneys as distinguished from double kidneys. The resections were done for the following lesions:

Stones	5 cases
Solitary cyst	1 case
Solitary cyst and stone	1 case
Traumatic cyst	1 case
Benign tumor	1 case
Carbuncle	1 case

Resection of one-half of a double kidney was done in six cases. It has frequently been stated that kidneys which are the seat of con-

genital anomalies are more prone to undergo pathologic changes than are normal kidneys. The six resections of double kidneys were done for the following lesions:

Hydronephrosis	3 cases
Hydronephrosis and stones	1 case
Hydronephrosis and ectopic ureter	1 case
Hydronephrosis and stone in ureter	1 case

INDICATIONS FOR RESECTION

1. Whether the solitary kidney is congenital in origin or the result of a previous nephrectomy, the problem of treating it when it becomes the seat of a serious lesion is the same. Among the lesions in a solitary kidney that are amenable to resection may be mentioned circumscribed collections of stones, especially with infection, the presence of a stone in a calix with dilatation and with a stricture of the *neck,* a hydronephrosis with more or less destruction of parenchyma, and encysted stones with abscess formation that lead to destruction of the parenchyma. Naturally, when these conditions are present in one of two kidneys, resection may just as well be performed.

2. In cases of bilateral stone in which one pole is diseased, or in cases in which there exists a circumscribed stone with pus formation.

3. In cases of partial hydronephrosis of the upper or lower pole with stone formation.

4. In cases of solitary cyst of the kidney. In this group of cases resection is at present recognized as the operation of choice and, as a rule, is very simple and easy of execution.

5. In cases of double kidney with double pelvis in which one-half shows the presence of hydronephrosis, severe infection, or stone.

6. In certain cases of metastatic kidney infection, that is, carbuncle of the kidney. Resection in a case of this sort proved to be a very wise choice in which the opposite kidney became the seat of a carbuncle. This case had many interesting phases (Case 10).

7. Poor function of opposite kidney.

In the following table is a summary of the ages of the patients upon whom a resection of the kidney was done.

TABLE OF AGES

Under 10 years	3 cases
10-20 years	1 case
20-30 years	3 cases
30-40 years	2 cases
40-50 years	3 cases
50-60 years	3 cases
Over 60 years	1 case
Oldest patient	61 years
Youngest patient	6 years

Group I: Cases of normally formed kidneys in which a resection was done.

RECURRENT RIGHT RENAL CALCULI

Case 1.—D. W. R., male, aged forty-six years, was admitted to the Presbyterian Hospital, July 8, 1928.

The symptoms began twenty-two years ago with left renal colic. The attacks would subside with the passage of gravel. The patient would then remain symptom-free for a period of four to five years when another attack would occur. He also experienced attacks of colic on the right side. Twelve years later, after having received injections of oil in the left ureter, a stone passed. Two years later stones were removed from the right kidney.

For the past five years and up to the present admission to the hospital the patient has complained of a pain in the right kidney region for which he sought relief.

Physical examination revealed nothing of importance.

Urinalysis report was: sugar 0, albumin 0, pus +.

Examination of blood gave the following count: red cells 4,850,000, leukocytes 9,900, hemoglobin 88 per cent.

Blood chemistry report was: Urea nitrogen 12.2, uric acid 2.8, creatinin 1.5, non-protein nitrogen 37.2.

Blood pressure was 122/72.

Wassermann test gave negative findings.

Roentgen-ray examination revealed within the right kidney area a large irregular density, apparently a kidney stone filling the pelvis and two shadows in the lower pole.

Cystoscopic examination revealed a mild cystitis. The bladder was otherwise normal. Both ureters were catheterized without difficulty or obstruction. Examination of the urine obtained at this time showed the following:

	Leukocytes per cu. mm.	Cultures
Bladder	66	B. Proteus
Right kidney	21	B. Proteus
Left kidney	13	Sterile

Phthalein test showed an output of 74 per cent of the dye for one hour.

Operation performed July 11, 1928, under ethylene anesthesia con-

sisted of (1) pyelotomy and removal of a large stone from the pelvis; (2) resection of the lower pole of the kidney. In the resected piece of kidney a very large cavity was found that contained two stones.

Recurrent stones in this case were probably due to the fact that when the stones were previously removed a cavity was left behind so that the patient again developed stones in his kidney.

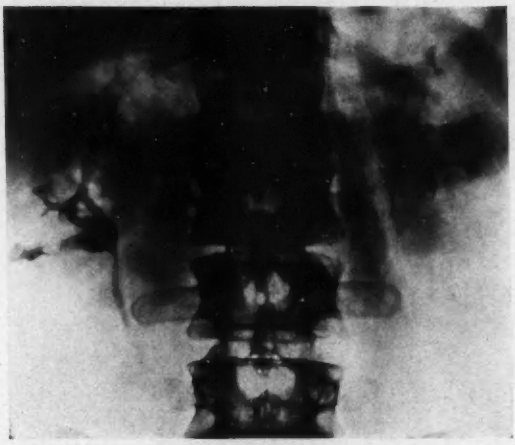


Fig. 1. Case 1. Pyelogram after resection of the kidney.

Recovery was uneventful. Subsequent roentgen-ray examinations were always negative for stone.

LEFT RENAL CALCULI

Case 2.—H. W., male, aged thirty years, was admitted to the Presbyterian Hospital, June 26, 1929.

Attacks of pain in the left kidney region associated with nausea and vomiting began seven years ago. Pain radiated along the course of the ureter. There was no hematuria, no frequency of urination, nor nocturia. X-rays at that time showed a stone in the left ureter which the patient passed two weeks later. The patient had no further trouble until two weeks ago when he was seized with a pain over the left kidney region which lasted for twenty-four hours.

Physical examination gave no positive information.

Urinalysis report was: Sugar 0, albumin 0, blood +, occasional leukocyte and many red blood cells.

Examination of blood gave the following count: Red cells 4,720,000, leukocytes 12,000, hemoglobin 85 per cent.

Blood chemistry report was: Urea nitrogen 18.3, uric acid 3.9, creatinin 1.9, non-protein nitrogen 39.7.

Wassermann test gave negative findings.

Roentgen-ray examination revealed a group of shadows in the region of the lower pole of the kidney on the left side.

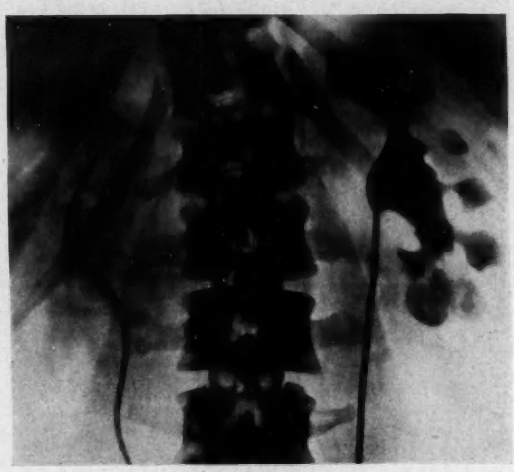


Fig. 2. Case 2. Pyelogram showing the presence of a large cavity in the lower pole of the kidney. Stones found in this cavity.

Cystoscopic examination revealed a normal bladder. Both ureters were catheterized without difficulty or obstruction. Examination of the urine obtained at this time showed:

	Leukocytes per cu. mm.	Casts	Cultures	Tubercle Bacillus
Bladder	50	0		0
Right kidney	20	0		0
Left kidney	80	Few granular		0

In guinea-pig tests of the bladder, the right and left pigs were negative for tuberculosis.

Left pyelogram showed a rather large pelvis; calices clubbed; inferior calix broad, not so densely filled as the rest and showing some mottling due to the stone shadows (Fig. 2).

Operation performed July 8, 1929, under nitrous oxide and ether consisted of resection of the lower pole of the kidney. This contained a large cavity in which eight stones were found.

Recovery was uneventful. Subsequent roentgen-ray examination showed a complete absence of the nest of calculi previously shown near the lower pole of the kidney. The last examination (March 16, 1934) showed no stone shadows. Blood chemistry report, May 10, 1934, was: Urea nitrogen 30, creatinin 1.71, non-protein nitrogen 52.

RENAL CALCULI AND URETERAL CALCULI

Case 3.—Dr. P. P., male, aged thirty-four years, was admitted to the Presbyterian Hospital, November 18, 1927.

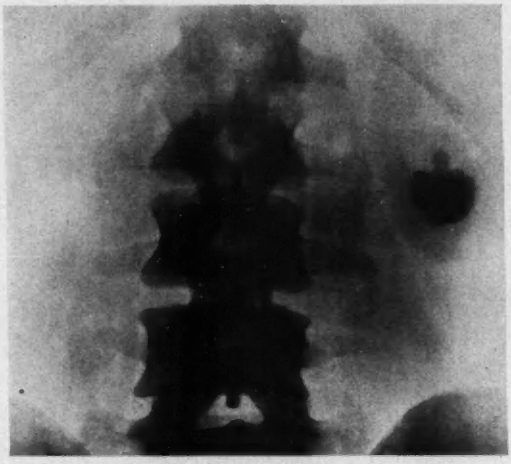


Fig. 3. Case 3. Note the peculiar shape of the stone in the lower pole of the kidney. At operation a large cavity with a narrow neck was found.

The patient had bilateral attacks of renal colic extending over a period of fifteen years, during which time more than twenty stones were passed. The attacks were associated with frequency, nocturia, urgency, burning and intermittent hematuria.

Seven years before he came under my observation, stones were removed from the right kidney. Two years later x-rays showed a recurrence of stones.

The attacks of renal colic and the passage of stones have continued up to the present time.

Physical examination revealed nothing of importance.

Urinalysis report was: Albumin 0, sugar 0, blood 0, leukocytes 60 per cubic millimeter.

Blood examination gave the following count: Red cells 4,786,000, leukocytes 14,400, hemoglobin 90 per cent.

Blood pressure was systolic 118, diastolic 78.

Roentgen-ray examination revealed bilateral kidney stones and two low-lying left ureteral stones.

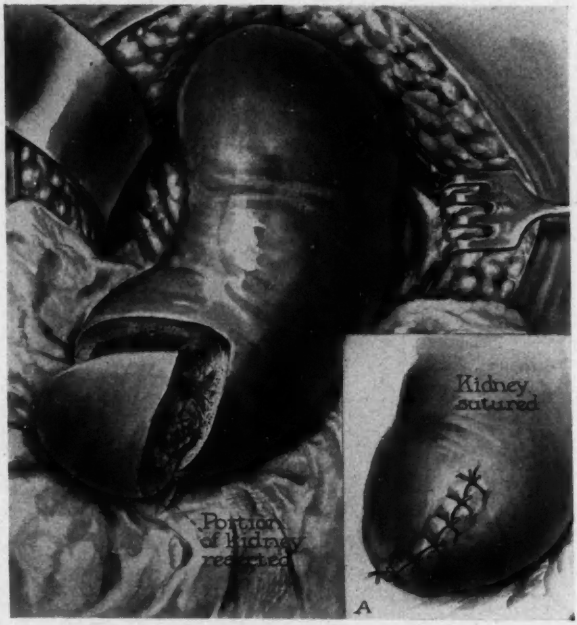


Fig. 4. Case 3. Wedge shaped piece resected, containing a large cavity with a dumb-bell type of stone. Insert (*A*)—Line of suture.

Cystoscopic examination revealed a normal bladder. Right and left ureters were catheterized without difficulty or obstruction. The urine obtained at this time showed:

	Leukocytes per cu. mm.	Cultures
Bladder	4	Sterile
Right kidney	3	Sterile
Left kidney	90	Sterile

Phthalein test showed a total output of 2 per cent from the right side and 5 per cent from the left side in twenty minutes.

Roentgen-ray examination revealed a large stone in the lower pole of the left kidney and two stones in the pelvic portion of the ureter. The stone in the kidney consisted of a very large lower part and an isthmus which was connected with a smaller part of the stone. This stone may be said to have a dumb-bell configuration (Fig. 3).

Treatment consisted of ureteral catheter and oil injections over a period of four months, during which time one of the stones was passed. The attacks of renal colic recurred more frequently and became more severe. Operation was advised.

On March 16, 1928, under ethylene anesthesia ureterotomy was done and the stone removed from the left ureter.

A second operation performed March 30, 1928, under ethylene anesthesia consisted of resection of the lower pole of the left kidney (Fig. 4).

It seemed to me that resection of the kidney was clearly indicated because of the large cavity with a narrow neck that would have remained if only the stone had been removed.

Convalescence was uneventful.

MULTIPLE RENAL CALCULI (RIGHT)

Case 4.—C. C., male, aged twelve years, was admitted to the Children's Memorial Hospital, November 9, 1932.

At the age of four months the infant entered the hospital because of difficulty and pain on urination for which a circumcision was done.

When admitted, he was suffering from a right-sided abdominal pain, nausea, vomiting and fever. A diagnosis of acute appendicitis was made.

Physical examination revealed a generalized rigidity of moderate degree over the entire abdomen, but especially over the upper right quadrant. Tenderness was noted over the entire right side, and a point of *severe* tenderness 1.5 cm. above McBurney's point.

Urinalysis report was: Albumin +, acetone ++, benzidine ++, 10 to 12 red blood cells per high power field, an occasional leukocyte, numerous cystin crystals, no casts; no bacteria in stained specimen.

Blood examination gave the following count: Leukocytes 19,650, polymorphonuclears 84 per cent, lymphocytes 11 per cent.

Roentgen-ray examination revealed two stone shadows opposite the transverse process of the first lumbar vertebra on the right side.

An intravenous pyelogram showed a slight delay in visualization of the dye on the right side and dilatation of the pelvis and ureter. The kidney and ureter on the left side were normal. There was increased density of the shadows in the region of the right kidney stones.

Operation performed November 25, 1932, under ether anesthesia, consisted of resection of the upper third of the kidney (Fig. 5), in

which was found a large cavity, containing stones, with a narrow outlet.

Chemical examination of the stones revealed pure cystin. Subsequent examinations of the urine during the patient's stay in the hospital showed no cystin.

Recovery was uneventful and the patient was discharged December 12, 1932.

Examination of the urine, April 27, 1933, showed cystin crystals. Chemical test for cystin was positive.

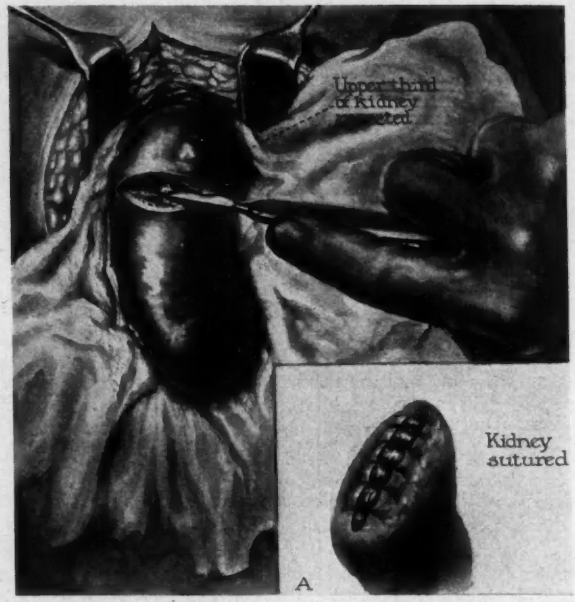


Fig. 5. Case 4. Resection of the upper third of the kidney. The resected portion of the kidney contained a large cavity with multiple stones. Insert (*A*)—Line of closure.

MULTIPLE KIDNEY STONES WITH DILATION OF THE INFERIOR CALIX

Case 5.—Dr. H. R., male, aged thirty-nine years, was admitted to the Presbyterian Hospital, June 2, 1932.

The first attack of right renal colic began fifteen years ago. Subsequent attacks were severe and required morphine for relief. Following the second attack a stone was passed. A roentgenogram three years

ago showed three stones in the right kidney. During the past three years there has been a fairly constant right lumbar backache. Two or three mild attacks of chills with fever have occurred during the past two years and varying amounts of pus and an occasional red blood cell have been found in the urine.

Physical examination revealed tenderness on deep pressure in the right costal vertebral angle. The lower pole of the right kidney was palpable and tender. There was bilateral incomplete direct inguinal hernia.

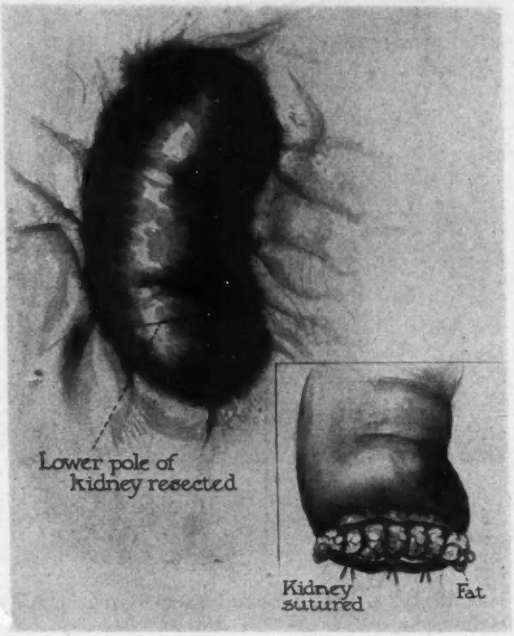


Fig. 6. Case 5. Resection of lower pole of kidney.

Urinalysis report was: Albumin 0, sugar 0, blood 0, leukocytes occasional; no red blood cells nor casts seen microscopically.

Examination of blood gave the following count: Red cells 5,120,000, leukocytes 8,600, hemoglobin 90 per cent.

Blood pressure was systolic 192, diastolic 90.

Roentgen-ray examination revealed three stones in the region of the

lower pole of the kidney. Two of the stones were covered by the shadow of the last rib.

Phthalein test showed a total output of dye, 56 per cent for one hour.

Operation performed June 3, 1932, under ethylene anesthesia, consisted of resection of the lower pole of the kidney which revealed a large cavity containing stones (Fig. 6).

Recovery was uneventful. Subsequent roentgen-ray examination (January 10, 1933) showed no signs of calculi at any point. The right kidney outline looked the same as in the picture of a year ago. Blood

Fig. 7. Case 6. Intravenous pyelogram showing deformity of the pelvis with mesial displacement of the ureter and outline of the cyst.

chemistry, May 10, 1934, was: Urea nitrogen 14, uric acid 5.4, creatinin 1.4, non-protein nitrogen 33.

SOLITARY CYST

Case 6.—Mrs. E. G., aged forty-five years, was admitted to the Presbyterian Hospital, June 1, 1932.

In June, 1930, a vaginal hysterectomy was done, and the following October a dull aching pain was noticed in the left side of the abdomen at the level of the umbilicus that radiated through to the back. The pain was intermittent; for weeks at a time it was completely absent, and then recurred and remained constant for several days or weeks.

After an interval of two months during which the pain was absent, a similar attack occurred, more severe in character. There were no urinary symptoms.

Physical examination revealed nothing of importance except a cystic swelling of the thyroid and an enlarged left kidney which was smooth, not tender, and freely movable. The right kidney was not palpable.

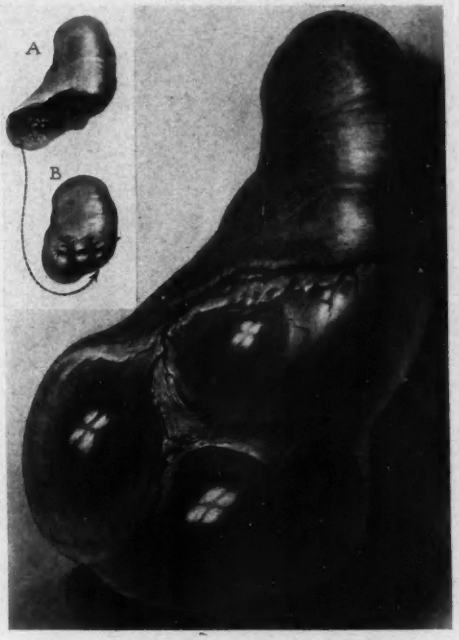


Fig. 8. Case 6. Large solitary cyst springing from lower pole. Insert (*A*)—Appearance of kidney after resection of cyst. (*B*)—Line of closure.

Urinalysis report was: Albumin 0, blood 0, sugar 0, a few red blood cells present in the sediment.

Blood examination gave the following count: Red cells 4,360,000, leukocytes 11,000, hemoglobin 84 per cent.

Blood chemistry report was: Urea nitrogen 11, uric acid 3.1, creatinin 1.4, non-protein nitrogen 34.

Blood pressure was: Systolic 134, diastolic 76.

Roentgen-ray examination revealed no stone. A large swelling was visible which was attached to the lower pole of the left kidney. The findings were compatible with a solitary cyst springing from the lower pole of the kidney.

Left pyelogram showed the pelvis and calices pushed up by the tumor mass in the lower pole so that the calices were compressed in the

Fig. 9. Case 6. Intravenous pyelogram after removal of cyst, showing a slightly distorted pelvis.

medial portion and drawn outward at the upper portion of the upper pole (Fig. 7). Right pyelogram revealed a normal condition.

Cystoscopic examination showed a normal bladder. Ureters were catheterized without difficulty or obstruction. Examination of the urine obtained at this time showed:

	Leukocytes per cu. mm.	Culture
Bladder	0	Sterile
Right kidney	0	Sterile
Left kidney	0	Sterile

Operation performed June 9, 1932, under ethylene anesthesia consisted of the usual left lumbar incision. A large solitary cyst about the size of a grapefruit was found springing from the lower pole of the kidney. The cyst was resected and a nephropexy was done (Fig. 8).

Recovery was uneventful. Intravenous pyelogram, July 18, 1933, showed a slightly distorted pelvis on the left side (Fig. 9). The right side was normal.

SOLITARY CYST OF THE KIDNEY. STONE IN THE KIDNEY PELVIS

Case 7.—M. S. G., aged sixty-one years, was admitted to the Presbyterian Hospital, October 22, 1928.

Chief complaint was hematuria. About three months before entering the hospital, the patient had noticed that the urine contained blood. This was not accompanied by pain and he thought that it was due to a strain. A roentgen examination at that time showed the presence of a stone in the left kidney. The urine cleared up in about a week and no blood had been noticed until one week ago.

Pain over the left kidney had begun about six weeks before and was described as a dull sore ache localized over the left kidney region. There was no radiation; the pain was not severe and bore no relation to urination, respiration or bowel movement.

Physical examination gave no important information.

Urinalysis report was: Albumin 0, sugar 0, blood +. Microscopic examination of the sediment revealed a few red blood cells.

Blood examination gave the following count: Red cells 4,460,000, white blood cells 7,400, hemoglobin 85 per cent.

Blood pressure was: Systolic 104, diastolic 68.

Blood Wassermann test gave negative findings.

Blood chemistry report was: Urea nitrogen 23.5, uric acid 4.4, creatinin 2.2, non-protein nitrogen 49.5.

Roentgen-ray examination showed the right kidney outline to be normal. The left kidney outline was normal except for a globular projection at the lower pole which was visible on several films. There was a dense shadow due to a stone in the region of the inferior calix.

Pyelogram showed the left kidney to be normal.

Cystoscopic examination disclosed a small median bar. The bladder was otherwise negative. Both ureters were catheterized without difficulty or obstruction. Examination of the urine obtained at this time showed:

	Leukocytes per cu. mm.	Cultures	Tubercle Bacillus
Bladder	10	Sterile	0
Right kidney	20	Sterile	0
Left kidney	20	Sterile	0

Phthalein test showed a total output of the dye, 20 per cent in thirty

minutes on the right side; 17.5 per cent in thirty minutes on the left side.

Operation was performed May 8, 1929, under ethylene anesthesia. The stone was removed through a pyelotomy incision. The cyst was resected (lower pole).

Recovery uneventful. Blood chemistry report May 10, 1934, was: Creatinin 1.2; non-protein nitrogen 36.3.

TRAUMATIC CYST OF LOWER POLE OF THE RIGHT KIDNEY

Case 8.—L. C., male, aged fifty-four years, was admitted to the Presbyterian Hospital, June 2, 1930.

Five months ago, while at work, the patient fell from a height of six feet and struck his right side against a roll of paper. He was able to walk, was taken home and then to a hospital, where he remained for fourteen days. He has been unable to work since the injury. Following the fall, blood in the urine was passed, accompanied with pain of a severe nature in the right upper quadrant and aggravated by movement. The pain was still present, but not so severe as it was immediately after the injury.

Physical examination revealed marked right costovertebral tenderness and slight rigidity of the right rectus muscle.

Urinalysis report was: Sugar 0, albumin 0, blood ++. Microscopic examination of the sediment showed many red blood cells and no casts.

Examination of blood gave the following count: Red cells 5,300,000, white cells 8,750, hemoglobin 82 per cent.

Blood chemistry report was: Urea nitrogen 20, uric acid 4.6, creatinin 1.3, non-protein nitrogen 45.5.

Wassermann and Kahn tests gave negative findings.

Roentgen-ray examination revealed no evidence of stone in the urinary tract.

Right pyelogram showed a filling defect compatible with tumor. The left pyelogram showed a normal condition.

Cystoscopic examination revealed normal bladder and ureteral orifices. The urine from the right and left kidneys and from the bladder was free of pus and sterile upon culture.

The findings in the intravenous pyelogram were verified by a retrograde pyelogram.

Because of the presence of a filling defect on the right side, obtained both with an intravenous and a retrograde pyelogram, a diagnosis of tumor—probably hypernephroma—was made and operation was advised.

Operation performed June 18, 1930, under ethylene anesthesia consisted of an unusual oblique kidney incision. Isolation of the kidney was extremely difficult on account of dense adhesions. A cyst the size of a large orange was found springing from the lower pole of the

kidney. Resection of the cyst with a small amount of kidney tissue was done.

Recovery was uneventful. A right pyelogram was made on April 21, 1931, and this showed a rather small but otherwise normal kidney pelvis.

ADENOMA OF THE KIDNEY

Case 9.—Miss F. M., aged twenty-four years. In June, 1920, the patient noticed an enlargement on the right side of the abdomen but did not consider it of sufficient importance to consult a physician. Three or four months later she called the attention of her family physician to the swelling because of its size. No pain or discomfort or any systemic disturbance occurred until within the last few weeks, when there were transient, slight aching pains and discomfort on the right side. The mass, according to her statement, progressively increased in size and at no time were large quantities of urine passed.

Physical examination was made March 25, 1924. Abdominal examination disclosed a large firm tumor mass which occupied almost the entire right half of the abdomen, extending from about 2 inches above the pelvic brim to the costal arch and medially to the midline. The mass was globular in shape, moved with respiration, was not painful upon palpation, and was about 10 inches in diameter. There was no evidence of fluctuation.

Blood examination gave the following count: Red blood cells, 4,000,000 leukocytes 6,700, hemoglobin 95 per cent.

Blood pressure was systolic 115, diastolic 75.

Urinalysis report was: Urine cloudy, acid reaction, albumin +, some blood cells, pus +++, no sugar, no casts, some epithelial cells.

Roentgen-ray examination showed the right kidney region to be covered by a large soft parts shadow which extended from the eleventh rib to the crest of the ilium and suggested a much enlarged kidney shadow.

Cystoscopic examination revealed normal bladder and ureteral orifices. Both ureters were catheterized without difficulty or obstruction. Examination of the urine obtained at this time showed:

	Leukocytes per cu. mm.	Urea	Culture	Casts	Red blood cells
Bladder	50		Sterile	0	++
Right kidney	90	1.05%	Sterile	0	++++
Left kidney	70	.87%	Sterile	0	0

Phthalein test resulted as follows:

	Right	Left
First 15 minutes	5%	12%
Second 30 minutes	8%	18%
Total 45 minutes	13%	30%

Pyelogram (right) revealed slight clubbing of the calices. In the

lying position, the pelvis was opposite the first lumbar vertebra; standing, the pelvis was opposite the fourth lumbar vertebra.

Diagnosis was tumor of the right kidney.

Operation performed March 28, 1934, under ethylene anesthesia consisted of resection of the tumor and nephropexy.

Convalescence was uneventful.

Histologic examination verified the diagnosis as adenoma of the kidney.

CARBUNCLE OF THE KIDNEY

Case 10.—J. R., male, aged eight years, was first admitted to the Presbyterian Hospital, September 17, 1932. At this time a diagnosis

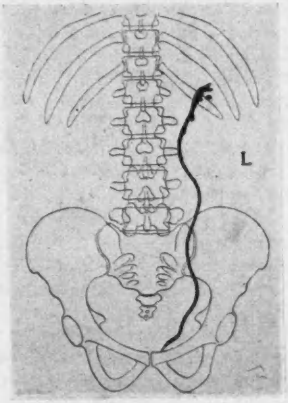


Fig. 10. Case 10. Retrograde pyelogram, showing deformity due to a carbuncle of the lower pole of the kidney.

of acute pyelitis, due to the staphylococcus aureus, was made. The patient was treated with pelvic lavage (1 per cent solution of silver nitrate) and was discharged as cured on November 3, 1932.

The patient was admitted a second time to the hospital, February 21, 1933, with chills and fever and the presence of a mass in the left flank, fever, leukocytosis, and some frequency of urination. A diagnosis of an acute perinephritic abscess was made. The abscess was drained on March 1, 1933, and the patient discharged on April 18, 1933.

The third admission to the hospital was on May 31, 1933. The patient was readmitted to the hospital because of a persistent sinus

in the left flank, tenderness on palpation, and a daily rise of temperature (103°).

Retrograde pyelogram (Fig. 10) showed a streak of the dye in the region of the left superior calix. The kidney pelvis and calices were obscured except for this streak, which seemed to be curved upwards by a mass which involved the lower two-thirds of the kidney.

Urinalysis report showed negative findings. Leukocytosis count was 24,700.

Operation, performed June 5, 1933, under ethylene and ether anesthesia, consisted of resection of lower half of the left kidney.

Convalescence was uneventful.

The patient was admitted to the hospital a fourth time, August 16, 1933.

Since leaving the hospital about six weeks ago, the patient had had no pain, but ten days ago began running an afternoon temperature of over 100°. For this reason he again entered the hospital.

Physical examination revealed extreme tenderness and rigidity to deep palpation on the right side of the abdomen. The impression conveyed was of a rounded mass deeply situated in the right upper portion of the abdomen. There was no tenderness in the left half of the abdomen.

Intravenous pyelogram showed a progressive filling of the right kidney pelvis and calices; very little at first, well filled and dilated on the last film. Pyelogram outline on the right extended through the width of three vertebræ. The left showed a small amount of media opposite the first lumbar vertebra and in the ureter. The kidney pelvis and calices were not outlined and seemed distorted.

Operation performed September 26, 1933, under ethylene and ether anesthesia consisted of an incision made over the right kidney. A perirenal abscess was opened and drained.

The patient was discharged November 3, 1933.

The fifth admission to the hospital occurred November 20, 1933.

Eight days after leaving the hospital, a daily elevation of temperature recurred up to 101°, but there was no pain. The patient was readmitted to the hospital.

Physical examination revealed nothing of importance except for the right loin wound, which had considerable infected granulation tissue with some purulent discharge. There was no tenderness in the right flank.

Operation was performed November 25, 1933, under ethylene anesthesia. A large amount of granulation tissue was removed with a curette from the site of the old incision in the right kidney. In the upper end of the wound a large, deep cavity was curetted.

Because of the persistent rise in temperature it was deemed advisable to do another operation on the right kidney.

This operation was done January 3, 1934, under ethylene anesthesia

An incision was made over the draining wound and multiple abscesses in the kidney were incised and drained.

The patient made an uneventful recovery and was discharged March 2, 1934.

Group II: Cases of double kidneys in which a resection was done.

COMPLETE REDUPLICATION OF THE PELVIS AND URETER (LEFT) INFECTED HYDRONEPHROSES, UPPER HALF OF LEFT KIDNEY, AND HYDROURETER

Case 11.—Mrs. A. R., aged fifty years, first entered the Presbyterian Hospital, March 2, 1927.

The patient gave a history of having had urinary difficulties for seventeen years. In 1918 she had an appendectomy with "no relief"

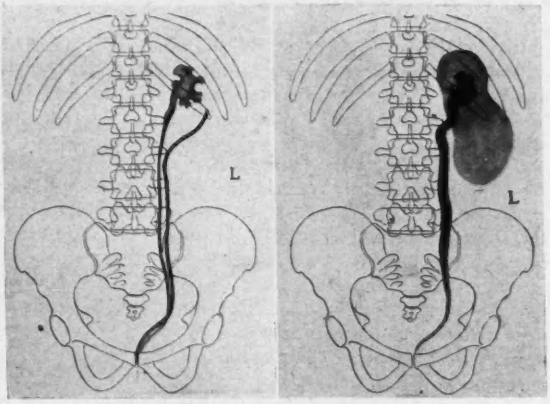


Fig. 11 *(left)*. Case 11. Moderate dilatation of the pelvis of the upper half of the kidney.
Fig. 12 *(right)*. Case 11. Marked increase in the dilatation of the ureter and pelvis.

of the symptoms, and within the next four years two operations were performed on the bladder for the removal of stones. She was free of symptoms for about two years, when the same symptoms gradually recurred. Upon admission to the hospital, she complained of pain when the bladder was full, pain across the back and left side, frequency of urination, nocturia, urgency and cloudy urine.

Physical examination revealed tenderness over the left upper quadrant and bladder region; otherwise negative.

Urinalysis report was: Sugar 0, albumin 0, blood 0, pus +++, 1 hyaline cast.

Examination of blood gave the following count: Red cells 4,800,000, leukocytes 12,300, hemoglobin 90 per cent.

Blood chemistry report was: Urea nitrogen 16.86, uric acid 4.44, creatinin 1.28, non-protein nitrogen 39.8.

Blood pressure was systolic 200, diastolic 120.

Wassermann test gave negative findings.

Roentgen-ray examination revealed no stone.

Cystoscopic examination showed a normal bladder. There were two ureteral orifices on the left side; the upper one appeared to be edematous. The right ureteral orifice was normal. Both ureters on the left side were catheterized without difficulty or obstruction. The urine at this time showed:

	Leukocytes per cu. mm.	Culture	Tubercle bacillus
Bladder	115	Staph. epidermis	0
Upper left ureter	586	Staph. epidermis	0
Lower left ureter	40	Sterile	0

Phthalein test (mixed) showed a total output of dye, 75 per cent in one hour.

Left pyelogram showed two pelves and two ureters that terminated in the bladder. In the upper pelvis and its corresponding ureter dilatation was marked. The lower pelvis and its ureter were normal (Fig. 11). Right pyelogram showed a normal condition.

Operation was advised and refused.

The patient re-entered the hospital five years later with the same symptoms and findings except for marked changes in the pyelogram (Fig. 12).

Operation performed March 4, 1932, under ethlyene anesthesia consisted of a heminephrectomy of the upper half of the double kidney. The ureter to the upper kidney was removed down to the brim of the pelvis. A nephropexy of the remaining portion of the kidney was done. At the upper third of the kidney was a line of constriction, above which the kidney showed marked dilatation and was soft and flaccid. There was one blood supply running into the lower half and one into the upper half.

Recovery was uneventful.

BILATERAL DOUBLE KIDNEY AND URETER; HYDROURETER OF THE UPPER HALF OF THE LEFT KIDNEY CONTAINING STONES; STONE IN THE LOWER HALF OF LEFT KIDNEY

Case 12.—Dr. J. E., aged fifty-one years, was admitted to the Presbyterian Hospital, October 2, 1933.

Symptoms began eighteen years ago with an attack of left renal colic, four months after which a stone was passed. Nine years later the patient was seized with an attack of severe renal colic on the left

side. After receiving dilatations of the ureter and injections of oil without results, the ureteral orifice was slit and the stone later passed.

The patient was symptom-free for eight years, when attacks of renal colic recurred on the right side associated with intermittent hematuria and pyuria. About one month later (eighteen months ago), he passed a stone, since which time the urine has continued to show large quantities of pus.

Five weeks before entrance to the hospital severe night sweats occurred, accompanied by chills, fever of 102°, and hematuria. Ten

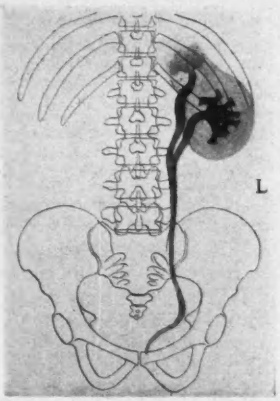


Fig. 13. Case 12. Dilatation of upper half of double kidney. Moderate dilatation of lower pelvis. Stones covered by neoskiodan.

days ago the patient experienced a sharp renal colic on the left side which was of short duration and associated with hematuria.

Physical examination revealed nothing of importance.

Urinalysis report was: Albumin 0, sugar 0, blood 0, leukocytes ++++.

Examination of blood showed the following count: Red cells 4,320,000, leukocytes 6,950, hemoglobin 95 per cent.

Blood chemistry report was: Creatinin 1.9, total non-protein nitrogen 33.3.

Blood pressure was: Systolic 138, diastolic 98.

Cystoscopic examination revealed a normal bladder. There were two normally placed ureteral openings. Both ureters were catheter-

ized without difficulty or obstruction. The urine obtained at this time showed the following:

	Leukocytes per cu. mm.	Gram smears		Tubercle bacillus
Bladder	720	Gram-positive cocci	Staph. albus	0
Right kidney	2	No organisms	Sterile	0
Left kidney	120	Occasional Gram-positive cocci	Staph. albus++	0

Phthalein test on the left side showed a total output of 3.5 per cent of the dye for one hour; right side, 6.5 per cent for one hour.

Intravenous pyelograms showed reduplication of the pelvis and ureter both on the right and left sides. The left upper pelvis showed dilatation and destruction of the calices; the stone shadows were covered by the media. The lower pelvis showed moderate dilatation (Fig. 13).

Operation was performed October 10, 1933, under ethylene anesthesia. A heminephrectomy was done, resecting the hydronephrotic upper half of the left kidney which contained stones. A pyelotomy of the lower half of the left kidney was done and two stones removed.

Recovery was uneventful.

DOUBLE KIDNEY (RIGHT)

HYDRONEPHROSIS OF UPPER HALF OF KIDNEY

Case 13.—Mrs. M. C., aged forty-one years, was admitted to the Presbyterian Hospital, October 31, 1923.

The patient had an attack of pain fourteen years ago for which she was given an injection of morphine, and since then has had attacks of pain in the loin occurring at irregular intervals. Associated with this pain she experienced pain in the bladder, at the external urethral orifice, and had frequency of urination. An attack of hematuria lasted for one day.

Physical examination revealed nothing of importance except that the lower pole of the right kidney was palpable and tender.

Urinalysis report was: Sugar 0, albumin 0, blood 0, pus +, motile bacilli.

Examination of blood gave the following count: Red cells 4,000,000, leukocytes 12,200, hemoglobin 82 per cent.

Blood chemistry report was: Urea 30.0, uric acid 3.0, creatinin 1.15, non-protein nitrogen 26.

Blood Wassermann test showed negative results.

Blood pressure was: Systolic 110, diastolic 78.

Roentgen-ray examination revealed no stone.

Cystoscopic examination revealed a normal condition of the bladder.

Right and left ureters were catheterized without difficulty or obstruction. Examination of the urine obtained at this time showed:

	Leukocytes per cu. mm.	Culture
Bladder	0	Colon bacilli
Right kidney	0	Sterile
Left kidney	0	Sterile

Phthalein test showed total output of the dye from the right kidney for thirty minutes, 1.5 per cent; from the left kidney, 8 per cent.

Right pyelogram showed reduplication of the kidney pelvis and ureter. Left pyelogram was normal.

Guinea-pig test of the bladder and right and left kidneys was negative for tuberculosis.

Operation was advised and refused.

Three years later the patient returned, complaining of severe attacks of pain. There was no essential change in findings. Operation was again advised.

Operation, performed June 3, 1926, under ethylene anesthesia, consisted of resection of the upper half of the double kidney (hydronephrosis).

Convalescence was uneventful.

DOUBLE KIDNEY AND DOUBLE URETER (LEFT)
HYDRONEPHROSES OF UPPER HALF OF KIDNEY AND HYDROURETER
ECTOPIC URETER

Case 14.—P. D., female, aged nine years, was admitted to the Children's Memorial Hospital, September 11, 1930.

Urinary dribbling had been present since birth. As a baby, the patient never had a dry diaper. It was thought the child would do better when older and trained, but these expectations were never realized. She urinated frequently and the urine could not be held for long periods of time; between urinations, there was constant dribbling. This condition had become more marked during the past two years.

Physical examination revealed nothing of importance except that over the middle of the sacrum in midline dorsally there was a defect in the bone that admitted two fingers. External genitalia were normal except that "just below the external urethral orifice was seen a small opening that discharged urine." A ureteral catheter was inserted into the opening and a prompt flow of urine was obtained.

Cystoscopic examination was carried out while the catheter was in place. A normal bladder and two normally located ureteral orifices were found. The ureters were catheterized without difficulty or ob-

struction. Examination of the urine obtained at this time showed the following:

	Leukocytes per cu. mm.	Cultures
Bladder	195	Bacillus pyocyaneus
Accessory ureter	157	Bacillus pyocyaneus
Left ureter	257	Bacillus pyocyaneus
Right ureter	325	Bacillus pyocyaneus

Urinalysis report was: Albumin ++, blood 0, sugar 0. Sediment showed pus and red blood cells.

Examination of blood gave the following count: Red cells 4,060,000, white cells 10,950, hemoglobin 80 per cent.

Roentgen-ray examination revealed no stone, but showed the presence of spina bifida occulta.

Left pyelogram, with shadowgraph catheters in place, showed that the ectopic ureter drained the upper half of the double kidney. There was a marked hydronephrosis in the upper half of the double kidney. The lower half was normal. The right pyelogram showed a moderate hydronephrosis.

Operation was performed October 2, 1930, under ether anesthesia. A heminephrectomy (left) was done with resection of the accessory ureter, which was dilated and tortuous.

Recovery was uneventful.

DOUBLE KIDNEY; HYDRONEPHROSIS; HYDROURETER OF UPPER HALF STONE IN URETER OF LOWER HALF RETROGRADE MOVEMENT OF THE STONE

Case 15.—G. H., male, aged twenty-two years, was admitted to the Presbyterian Hospital, December 29, 1931.

The patient was in good health up to five months ago, when he first had an attack of severe pain in the right lumbar region radiating to the right testicle and accompanied by gross blood in the urine. The attacks recurred at intervals of two to three weeks at first, and during the past few weeks almost daily, with three to four attacks on some days. The pain sometimes occurred only in the testicle. The hematuria was more pronounced during the early attacks than at present.

Physical examination revealed nothing of importance.

Urinalysis report was: Albumin +, sugar 0, blood ++; sediment, loaded with pus cells; no casts. Cultures showed B. pyocyaneus.

Examination of blood gave the following count: Red cells 4,310,000, leukocytes 26,400, hemoglobin 80 per cent.

Blood Wassermann and Kahn tests gave negative results.

Blood pressure was: Systolic 134, diastolic 60.

Roentgen-ray examination revealed a stone opposite the third lumbar vertebra on the right side. A subsequent roentgen-ray examination showed that the stone had wandered back up into the kidney and was located in the inferior calix.

Cystoscopic examination revealed a normal bladder. Two normally situated ureteral orifices were seen. They were catheterized without difficulty or obstruction. Examination of the urine obtained at this time showed:

	Leukocytes per cu mm.	Cultures
Bladder	9600	Bacillus pyocyaneus
Right kidney	80	Bacillus pyocyaneus
Left kidney	40	Sterile

Fig. 14. Case 15. Resected upper half.

On the right side, pyelogram showed moderate dilatation of the kidney pelvis and clubbing of the calices. The stone shadow was opposite the third lumbar vertebra. The left side was normal.

The intravenous pyelogram did not show the upper half of the double kidney on the right side. This was due to the fact that the upper half was completely destroyed. There was no secreting tissue present, hence visualization of the upper half of the double kidney was absent.

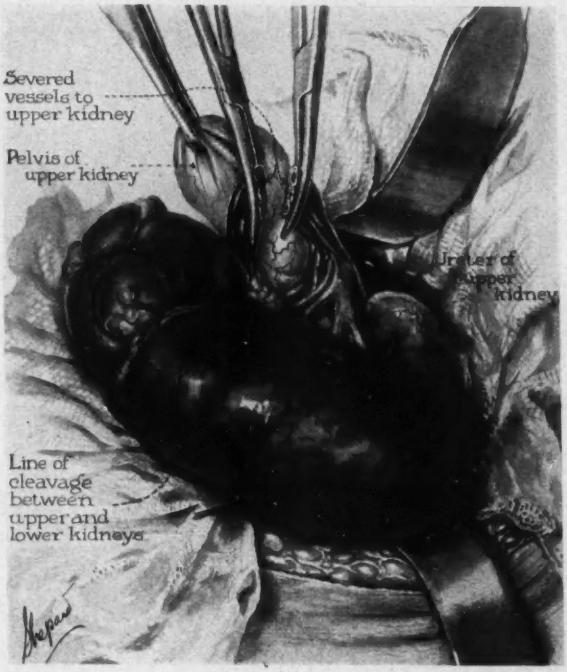

Severed vessels to upper kidney
Pelvis of upper kidney
Ureter of upper kidney
Line of cleavage between upper and lower kidneys

Fig. 15. Case 15. Note enormous dilatation of upper ureter and pelvis.

Operation was advised because the ureteral catheterization treatment failed to deliver the stone.

Operation was performed March 14, 1932, under ethylene and ether anesthesia. Two ureters and a double kidney were found. The upper half of the kidney was completely destroyed and the ureter enormously dilated (Fig. 14). Resection of the upper hydronephrotic half was carried out (Fig. 15).

A ureterotomy was done with removal of the stone from the ureter that drained the lower half of the double kidney.

Recovery was uneventful.

DOUBLE KIDNEY AND DOUBLE URETER (RIGHT) HYDRONEPHROSIS OF LOWER HALF OF KIDNEY AND HYDROURETER

Case 16.—J. P., female, aged six years, was admitted to the Children's Memorial Hospital, November 29, 1933.

The patient had always been in good health up to five months ago, when she first developed a dull, aching pain in the right kidney region. The pain was practically constant and at times worse at night, often causing her to cry and keeping her from sleeping. Occasionally she had fever, but there were no urinary symptoms. She has always had enuresis. The pain persisted for six weeks before she was taken to a doctor. There was some relief of pain with medication.

Physical examination revealed nothing of importance.

Urinalysis report was: Albumin +, blood +, sugar 0, pus +, and a few red blood cells.

Examination of blood gave the following count: Red cells 4,860,000, leukocytes 11,300, hemoglobin 86 per cent.

Blood chemistry report was: Non-protein nitrogen 29.

Blood pressure was: Systolic 120, diastolic 80.

Roentgen-ray examination revealed no stone.

Right pyelogram showed a streak of dye running from the last rib to the upper border of the fourth lumbar vertebra. Left pyelogram showed a normal condition.

Retrograde pyelogram (made elsewhere) showed much looping of the catheter in the right ureter. The ureter was dilated and formed a loop opposite the fourth lumbar. There was dilatation of the pelvis and calices.

The child developed a pharyngitis and bilateral otitis media, and a bilateral paracentesis was done. Further work on the kidney was postponed and the patient was discharged January 10, 1934.

On second admission, February 27, 1934, no essential change in condition was noted.

Operation performed March 1, 1934, under anesthesia consisted of a heminephrectomy of the lower half of the double kidney. The dilated ureter to the lower kidney was removed about 8 cm. from the pelvis. A nephropexy of the remaining portion of the kidney was done. There was a line of demarcation between the two portions of the kidney, and the lower half was composed of the markedly enlarged hydronephrotic sac with a shell of renal tissue.

Recovery was uneventful.

This case is interesting in that the lower half showed the pathology and was resected, which is the exception, since the upper half is embryonic and most frequently the seat of pathology.

My experience agrees with that of Herbst and Polkey, who found that the danger of hemorrhage and fistulæ were rare in the experimental animal.

The question of hemorrhage was not troublesome in this series of cases, either at the time of the resection or subsequently. In the cases of double kidney it was a relatively simple procedure to isolate the vascular supply to the diseased half and to ligate the vessels before the resection was done. If one follows this procedure the operation is practically bloodless.

In the ten cases of normally formed kidneys in which resection was done, there was no difficulty in controlling the bleeding with sutures. In none of these cases was the bleeding marked. In one case with a very slight oozing, a piece of fat was transplanted.

Reference to the possibility of a persistent postoperative urinary fistula has been mentioned by some authors. In this series there were no fistulæ. Careful suturing will, in all probability, prevent the occurrence of a postoperative fistula. When one of the calices has been opened great care should be exercised in its closure by careful suture.

The determination of the line of resection is generally quite simple. In the cases of double kidney a line of demarcation between the normal half and the pathologic half is readily discernible in most cases, although in a rare case such may be absent or poorly defined.

As a rule, in the cases of solitary cyst but little difficulty is experienced in finding a line of cleavage between the cyst and the kidney. Likewise in the one case of benign tumor reported in this paper, little difficulty was experienced in finding the line of cleavage and it was easily followed by blunt dissection.

In the cases of stone associated with the presence of a cavity, no line of cleavage can be demonstrated on the surface of the kidney. Great care was taken in the resections to remove these cavities completely.

In the stone cases two kinds of resections were carried out. In four cases the line of incision was carried out by cutting across the kidney from its outer to its inner border. In one case, in which the stone corresponded more or less to a dumb-bell in its configuration, a wedge-shaped resection of the kidney was done (Fig. 4).

BIBLIOGRAPHY

BARDENHEUER: Verhandl. Deutsch. Gesellschaft f. Chir., 2:111, 1891.
BLOCH: British Med. Jour., 2:1100, 1896.
CZERNY: Quoted by Herczel.
EISENDRATH, PHIFER and CULVER: Jour. Urol., 13:525, 1925.
HERBST and POLKEY: Surg., Gynec. and Obstet., 51:213, 1931.
HERCZEL: Beitr. z. Klin. Chir., 6:485, 1890.
JUDD: Ann. Surg., 82:458, 1925.
KEETLEY: British Med. Jour., 2:147, 1890.
KUMMELL: Deutsch. Gesellschaft f. Chir., 22:146, 1893; also Centralblatt f. Chir., 17:329, 1890.
MOYNIHAN: British Med. Jour., 1:263, 1902.
PETERS: Beitr. z. Klin. Chir., 129:716, 1923.
RATHBUN: Amer. Jour. of Surg., 13:565, 1931.
SPIEGELBERG: Arch. f. Gynækol., 1:146, 1870.
WAITZ: Deutsch. Med. Woch., 17:498, 1891.
WELLS: British Med. Jour., 1:758, 1884.
YOUNG: Surg., Gynec. and Obstet., 38:107, 1924.

THIRD DAY, MAY 16, 1934

TRANSURETERO-URETERAL ANASTOMOSIS

REPORT OF A CLINICAL CASE

CHARLES C. HIGGINS, M.D.

From the Cleveland Clinic, Cleveland, Ohio

The case I am about to report is of interest because, as far as I can determine from a thorough search of the literature, the operation described has never before been done on man. The only two articles that I encountered in the American literature were written in 1906 and in 1911. The first report, by Sharpe[2] of St. Louis, described experimental operations on dogs and cadavers, and the other, by Gilbride[1] of Philadelphia, described an operation on a cadaver. Both of these investigators proved that such an operation was an anatomic possibility, but the case here reported furnishes the first proof that the operation is physiologically successful in man.

The problem presented in this case was so unusual that it was hard to decide what surgical procedure to employ.

The patient, a young man, aged twenty-five years, had had rather a stormy course for about a year, since he had begun to suffer from frequency, urgency and nocturia, and also pain in the region of the right kidney while voiding. Four or five months after these symptoms appeared, a cystotomy had been performed by another surgeon. At this operation several small calculi were removed from the bladder and a large diverticulum containing stones was found, involving the right side of the bladder. The stones were removed, but the diverticulum was left intact. The same symptoms persisted after this operation.

Four months later, the patient experienced an attack of severe pain over the bladder area associated with a chill and fever and I was called in consultation. I then operated on the patient and found that the diverticulum had ruptured and that there was a large accumulation of urine, pus, and numerous small calculi between the peritoneum and the bladder in the pelvis. Diverticulectomy was performed and the patient's convalescence was uneventful. He gained 12 pounds and the urinary symptoms subsided with the exception of pain in the region of the right kidney on attempting to void. The pain was so severe that after voiding he would have to lie down. At that time a catheter-

ized specimen from the kidney and bladder was free from pus and organisms. The other laboratory findings were normal. Cystoscopic examination showed hypertrophy of the trigone which was producing some obstruction. This was then resected, but the symptoms persisted.

The patient, then, when attempting to void, still had a reflux up to

Fig. 1. Cystogram before operation.

the right kidney pelvis which was producing excruciating pain and gradually was producing a hydro-ureter and hydronephrosis (Figs. 1 and 2). The question arose as to the logical surgical procedure that should be employed. Ordinarily three technics were available: (1) nephrectomy, (2) re-implantation of the ureter into the bladder, or (3) transplantation of the ureter into the rectum.

Since the kidney was not infected and still had good function (Fig. 3), nephrectomy seemed unwise. The previous diverticulectomy had caused the peritoneum to adhere closely to the bladder, and a suitable site for re-implantation was lacking. Leakage might occur into the abdominal cavity were this procedure to be employed. Finally, I hesi-

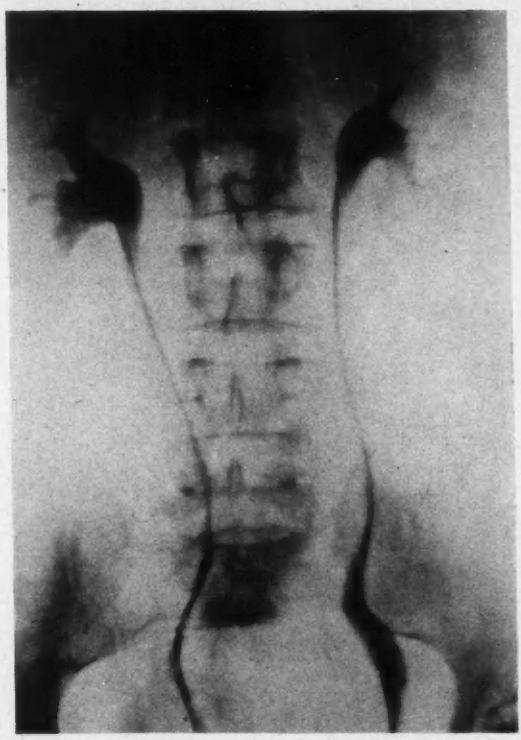


Fig. 2. Pyelogram before operation.

tated to transplant the one ureter into the rectum, transforming the patient into neither bird, beast, nor man.

Dr. Lower saw this patient with me in consultation, and we decided that this was an ideal case for transuretero-ureteral anastomosis, especially since there was a suitable site for re-implantation of the right ureter at the point of the dilatation of the left ureter and it appeared

as though the operation could be performed without danger of stricture or impairment of function of the left kidney. The technic of the operation was as follows:

With the patient in the Trendelenburg position, the abdomen was opened through a midline incision. After the intestines were packed away, the right ureter was identified as it passed over the brim of the pelvis. An incision about 2 inches long was made in the posterior parietal peritoneum, bringing the right ureter into direct view. It was then freed from its bed down to within one-half inch of the bladder.

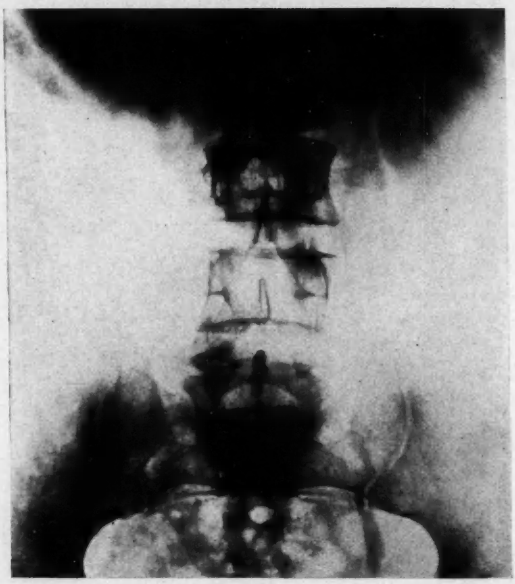


Fig. 3. Intravenous urogram before operation.

Here it was doubly clamped, divided and ligated. The proximal end was fully isolated for a distance of about 3 inches. The left ureter was then identified and exposed at the site of dilatation by an incision in the posterior parietal peritoneum. The two ureteral catheters were palpable within the ureter.

By means of a curved clamp a tract was made posterior to the posterior parietal peritoneum from the right ureteral bed at the brim of the pelvis to the point in the region of the left ureter where the anastomosis was to be performed, where it was continued through the

peritoneum. The mobilized end of the right ureter was then brought through this new bed to be anatomosed with the left ureter.

A small longitudinal incision was made in the left ureter and one of the catheters was delivered through the opening. This end of the catheter was passed up through the open end of the right ureter to the kidney pelvis, acting as a splint. The free end of the right ureter was then anastomosed to the side of the left ureter with interrupted sutures of triple 0 chromic catgut. The incision in the posterior parietal peritoneum over the left ureter was then closed with interrupted sutures. The incision in the posterior parietal peritoneum was not

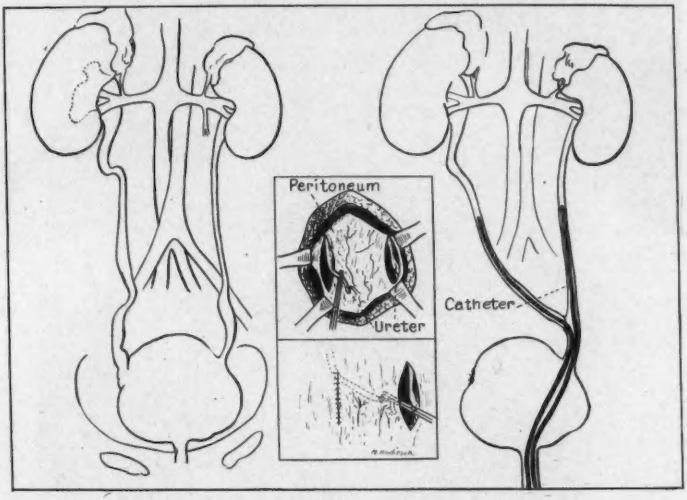


Fig. 4. Diagram of operation.

closed tightly. Drainage was established by a stab incision through the abdominal muscles to the region of the anatomosis. In this area a strip of rubber dam was placed over the site of anatomosis. The abdomen was closed in the usual manner (Fig. 4).

Convalescence was uninterrupted (Fig. 5). No urinary leakage occurred and the patient was discharged twelve days after operation. An intravenous urogram after operation showed prompt initial function of both kidneys, which later became a little slower on the left side (Fig. 6). The left ureter appeared normal below the pelvis of the kidney. Postoperative observations a year and a half after opera-

Fig. 5. Pyelogram day after operation.

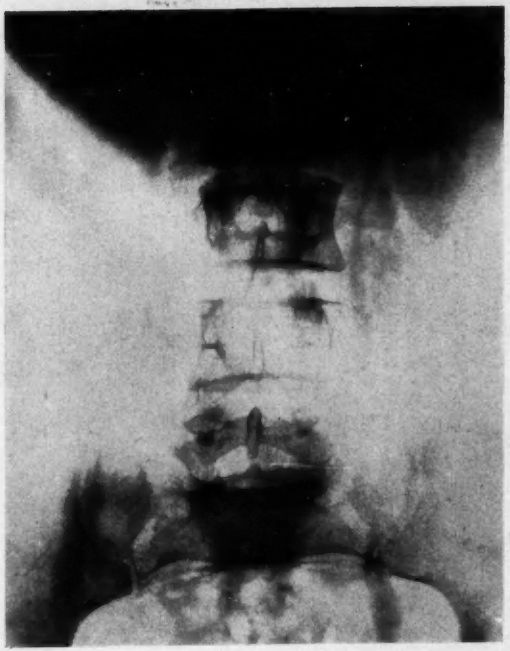


Fig. 6. Intravenous urogram after operation.

tion showed both kidneys to be functioning well with no evidence of obstruction at the site of the ureteral anatomosis (Fig. 7).

Although such a procedure may seldom be indicated, it is an anatomic and physiologic possibility and adds another conservative technic to the armamentarium in urologic surgery.

Fig. 7. Pyelogram one and one-half years after operation.

REFERENCES

1. GILBRIDE, J. J.: A new operation for ureteral anastomosis. Jour. Am. Med. Assn., 57:821-822 (Sept. 2), 1911.
2. SHARPE, N. W.: Transuretero-ureteral anastomosis. Ann. Surg., 44:687-707, 1906.

OPERATIVE INJURIES OF THE URETER

IRA R. SISK, M.D.
Madison, Wisconsin

Although a review of the literature reveals numerous reports of operative injuries of the ureters, it is probable that relatively few cases are recorded. This discussion deals briefly with the treatment of some types of such injuries and is based on the observation and treatment of five cases.

In considering the question of operative injury of the ureter either from the standpoint of prevention or treatment, the important thing to be kept in mind is the preservation of renal function. Before entering upon a discussion of the treatment of these injuries means of preventing them should be mentioned. The presence of a catheter in the ureter during difficult operations in the pelvis will make it possible to avoid the ureter easily. For many years we have routinely inserted catheters in the ureters of such patients for the Department of Gynecology at the Wisconsin General Hospital, and as a result only one ureter has been damaged (No. 4 of this series). In this case serious pathology was unexpectedly encountered and catheters had not been introduced.

In treating these injuries the genito-urinary surgeon encounters many difficult problems. The variations depend upon the age of the injury, its distance from the bladder, whether one or both ureters are involved, and the type of injury; that is, whether it is completely severed, completely severed with the removal of a segment, partially severed, ligated or clamped. Suddenly confronted with the problem of dealing with a severed ureter many surgeons adopt the procedure of ligation as the best way out of the dilemna. Embarrassing circumstances are in this way avoided in many cases, but a kidney is rendered functionless. Further, in some cases this treatment results after a lapse of a few days in urine draining from the ureter into the peritoneal cavity, or possibly finding its way to the outside, or infection in the kidney may necessitate surgical interference. The ligation of a cut ureter under circumstances favorable to repair should receive our most severe condemnation.

The method of repairing the ureter when the injury is discovered

at the time of operation is for obvious reasons of the greatest importance. However, since the genito-urinary surgeon is rarely present when the injury occurs he will seldom have to deal with this situation. Simple ligation is justified only when the condition of the patient is too bad to permit an operation for repair, which, of course, requires more time.

A large number of operations have been described for the repair of this type of injury, but all are based on the principles of end-to-end, end-in-end, or side-to-side anastomoses. As this operation will always be infrequently performed, a simple method should be adopted and its principles thoroughly understood, so that when called upon to repair a ureter the surgeon will not have to use a technic with which he is not thoroughly familiar. My first opportunity for repairing a severed ureter came suddenly. Fortunately, a satisfactory repair was made and a normally functioning kidney was obtained (Case 1). Afterwards in looking up the subject I found that I had adopted the technic described by Dr. Hugh Young. This technic seems to combine the principles of simplicity, splinting of the ureter, maintenance of caliber, and satisfactory drainage. It is, I believe, the technic of choice for the repair of these ureters with certain exceptions which will be mentioned later. The technic is as follows:

A ureteral catheter as large as will freely move through the ureter without interfering with the circulation is introduced into the ureter and passed into the kidney pelvis. Introduction may be made through a cystoscope or the catheter may be passed each way from the point of injury, the lower end being brought out through the urethra later. Over this catheter end-to-end anastomosis is made with fine catgut, the sutures being passed through the serous and muscular layers. With satisfactory drainage the catheter may be left in place for many days to prevent contraction of the lumen during healing.

Exceptions are to be made when (1) the injury is sufficiently low to permit re-implantation into the bladder, which is preferable; or when (2) a segment has been removed of sufficient length to cause tension. If there is tension satisfactory healing will not occur and implantation into the bowel is the operation of choice.

In old injuries every case is a law unto itself. After appropriate examinations to determine the condition of the kidneys and ureters a satisfactory procedure must be selected. This may be a plastic

repair, implantation into the bladder or bowel, nephrostomy, or nephrectomy.

Case 1.—Mrs. J. N., a white woman, aged twenty-four, was operated on April 9, 1929, by a general surgeon for an inflammatory mass of long standing which was located in the left side of the pelvis, having originated in the left fallopian tube. During the course of the operation it was discovered that the left ureter had been severed. Being in

Fig. 1. Case 1. Intravenous urogram made nearly five years after left ureter was completely severed and repaired. The kidney pelvis and ureter appear normal.

the hospital at the time, I was called, and with the wound still open passed a direct cystoscope into the bladder, and introduced a No. 6 catheter into the left ureter. When this catheter reached the point of severance the surgeon introduced it into the proximal end of the ureter and it was passed to the kidney pelvis. The ends of the ureter were then anastomosed, end to end, with fine chromic catgut sutures, which were passed through the serous and muscular layers. There was never any leakage of urine at the point of anastomosis. The

catheter was removed on the tenth day. Convalescence was smooth and uneventful. The patient was discharged from the hospital on the twentieth postoperative day in good condition. She has been seen at intervals since and has at no time had any symptoms referable to the kidney, and the urine has been normal. She was last seen in February, 1934, when she came for examination at my request. She

Fig. 2. Case 2. Retrograde urogram (reversed) showing normal right kidney and extravasation of medium in peri-ureteral tissues on left. This was made more than two months after the injury, the ureter having been repaired and the catheter left in the ureter for fifteen days after the operation.

was free of symptoms, the urine was negative, and intravenous urograms showed normal kidney pelves and ureters.

Case 2.—Mrs. B. was operated on by a general surgeon, August 11, 1931, for the removal of an ovarian cyst. About 4 cm. of the ureter which was attached to the wall of the cyst were removed. I was called at the time and inserted a No. 12 catheter through a cystoscope as described in Case 1. The ureter was repaired as in Case 1 but with considerable tension due to the removal of a piece of the ureter. On

the seventh day a small amount of urinary drainage was noted on the dressing. There was no further drainage and recovery seemed uneventful. The catheter, which had drained freely, was removed on the fifteenth day and the patient went home on the nineteenth day with the wound well healed. Ten days later, however, she developd symptoms of frequent and painful urination and the urine was found to contain considerable pus. She was treated for several weeks with bladder lavage and urinary antiseptics, but was returned to the hos-

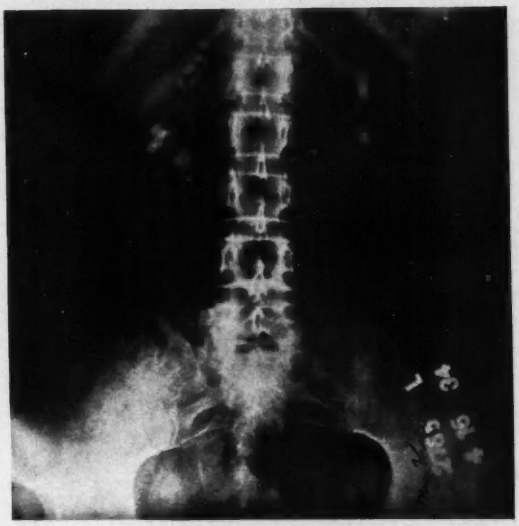


Fig. 3. Case 3. Intravenous urogram three years after re-implantation of injured left ureter into bladder. The pelvis, calices and ureter are normal or very slightly dilated.

pital on October 13, 1931, when she had a chill, fever, and pain in the right side of the abdomen. On cystoscopic examination the right kidney was found to be infected with B. coli. No urinary spurt was seen on the left side and though the left catheter apparently passed to the left kidney the urogram indicated that it passed into the periureteral tissues at the point of severance, where it was coiled. The proximal end of the ureter apparently healed with occlusion as an intravenous urogram showed no evidence of dye in the left kidney pelvis and ureter.

Case 3.—Mrs. H. K., a white woman, aged forty-eight, had a vaginal

hysterectomy and repair of cystocele by a general surgeon on March 24, 1931. Following the removal of a vaginal pack urine was noted from the vagina. From cystoscopic and other examinations it was determined that this was due to an injury to the left ureter. On October 7, 1931, through a left rectus incision the left ureter was isolated, freed, and re-implanted into the bladder. Convalescence was uneventful and the patient was discharged from the hospital on the twenty-first day in good condition. The patient has been seen at intervals since and has been free of symptoms referable to the urinary

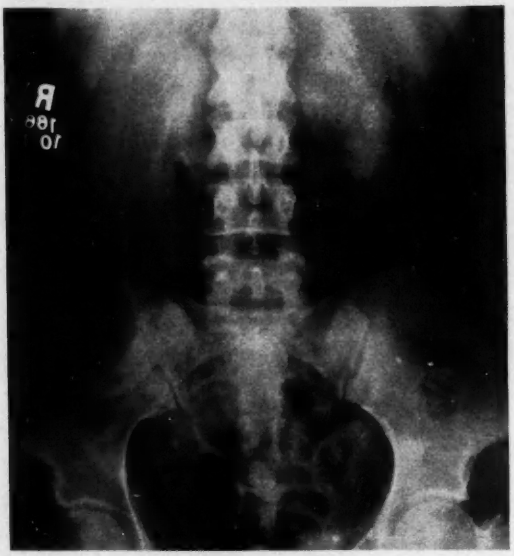


Fig. 4. Case 4. Intravenous urogram showing hydronephrosis on the side of injury (left).

tract. She was last examined on April 15, 1934, when she was free of symptoms and the urine was normal. An intravenous urogram at that time showed good function in both kidneys and very little dilatation in the left pelvis.

Case 4.—Mrs. C. M., a white woman, aged forty-six, was operated upon by a gynecologic surgeon in November, 1930, for a very large fibroid tumor. When ligating the left uterine vessels a structure thought to be a severed ureter was encountered. It was ligated, the abdominal wound was closed and vaginal drainage instituted. A few

days after operation urine began to drain through the vagina. Four weeks after operation an intravenous urogram revealed a large left hydronephrosis. A left nephrectomy was performed. Convalescence was uneventful. As large aberrant vessels were found going to both poles of this kidney, it is probable that the vessel to the lower pole was at least partly responsible for the hydronephrosis.

Case 5.—A white woman aged thirty-eight was first seen on June 24, 1931. She presented a letter from her local physician, who stated

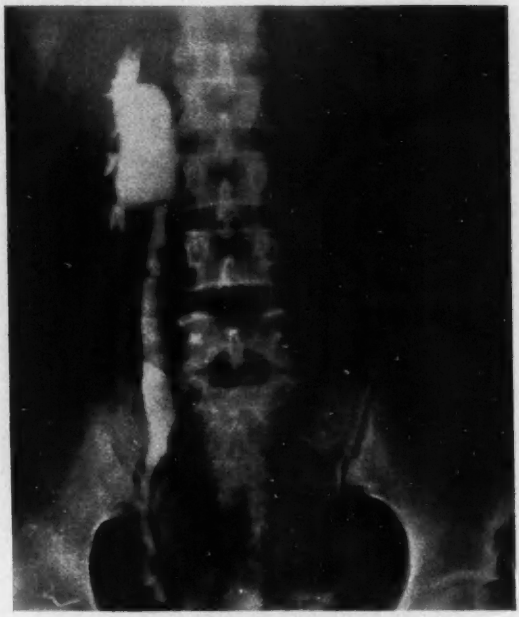


Fig. 5. Case 4. Retrograde pyelo-ureterogram (right).

that he performed an operation in March, 1931, for the removal of cysts from both broad ligaments. The left ureter was cut and repaired by invaginating the proximal end into the distal end. The wound healed, but ten days after discharge from the hospital severe chills and fever occurred, the wound re-opened and urinary drainage was noted. This continued. When we first saw the patient she was acutely ill with temperature 103-104, chills, fever, nausea and vomit-

ing. There was free urinary drainage through the old abdominal incision. Urine was voided regularly. On cystoscopic examination urine was seen spurting from the left ureter and indigo-carmine appeared in nine minutes. A catheter met an impassable obstruction 3 inches above the bladder. No urine was seen coming from the right ureter and indigo-carmine did not appear. A catheter met an impassable obstruction 5 inches above the bladder. A diagnosis was made of complete occlusion of the right ureter, probably result of ligation, and left uretero-abdominal fistula, part of the urine from the left

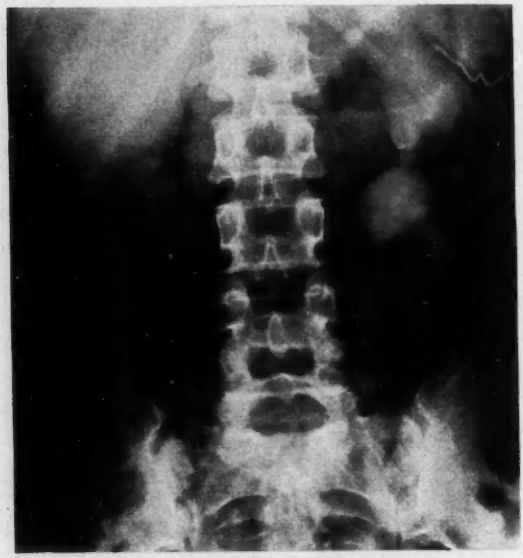


Fig. 6. Case 5. Intravenous urogram. The left pelvis, calices and ureter are moderately dilated. No dye was excreted by the right kidney.

kidney draining into the bladder and part through the fistula. Operation was performed on July 14, 1931. The left ureter was located and was found to be firmly adherent to the iliac artery for a distance of 1.5 inches; this was carefully dissected free. The fistulous tract which passed through the abdominal cavity was dissected from the ureter and the peritoneum was closed. The ureter was then opened above the strictured area and the stricture was widely dilated. Through the opening in the ureter a No. 12 catheter was passed upward to the kidney pelvis and downward through the bladder to the

outside. The ureter was sutured and the wound closed with drainage. As a result of the free drainage the patient's condition in a few hours was better than before the operation. The catheter drained freely in large quantities and there was no urinary drainage on the dressings.

The patient died suddenly on the third postoperative day, apparently from an embolus, though this could not be confirmed as autopsy was refused.

Fig. 7. Case 5. Bilateral ureterograms (retrograde reversed). Catheters could not be passed to kidneys as one ureter was completely occluded and the other was nearly occluded at the point of injury.

COMMENT

There are in the literature many case reports in which it is assumed that a satisfactory result has followed a ureteral repair, but few in which the question is proven by appropriate follow-up examination. In 1929 Curtis reported a case in which a satisfactory result followed an end-to-end anastomosis and stated, "I believe that this is the only recorded case in which end-to-end anastomosis of the ureter has been followed by clinical proof of normal

kidney-ureter function." To the successful proven cases we add Case 1, and as further proof of the well-known fact that the absence of symptoms following the repair of a ureter does not prove the result satisfactory, we cite Case 2, in which complete healing with occlusion occurred after the removal of an indwelling catheter which permitted free drainage from the kidney for fifteen days after the operation.

CONCLUSIONS

1. Normal kidney-ureter function may be obtained following complete severance of a ureter by end-to-end anastomosis over a ureteral catheter.

2. Simple ligation of a severed ureter is contra-indicated if the condition of the patient will permit a conservative operation.

3. The absence of symptoms following the repair of a severed ureter does not prove the result satisfactory.

4. In old injuries of the ureter a suitable procedure must be adopted to each case. Re-implantation into the bladder is desirable if possible. Implantation into the bowel, nephrostomy, or nephrectomy may be indicated.

BIBLIOGRAPHY

CURTIS, A. H.: The management of ureteral injuries with a discussion of the surgical indications in patients who require ureteral transplantation. Surg., Gynec. and Obstet., 48:320-323, 1929.

YOUNG, H. H.: Practice of Urology, Vol. II.

ECTOPIC VAGINAL URETER

CLYDE L. DEMING, M.D.

From the Department of Surgery, Yale University, and the New Haven Hospital, New Haven, Connecticut

The ectopic vaginal ureter has thus far evaded the annals of urologic literature except for a few isolated reports. It is the object of this paper to correlate the authentic cases, to add one new case and discuss the subject in detail with emphasis on an early diagnosis and treatment.

After reviewing many of the cases reported, the author has been obliged to read the original articles for authenticity. In many instances the copied reports were found to be incorrect. The ureters instead of emptying into the vagina opened around the external meatus, or their openings were not definitely located. Other cases reported failed to give convincing details in the history and in the operative findings to warrant this classification. Depaul reported the first ectopic vaginal ureter from an autopsy in a newborn child in 1852, while Emmett reported the first clinical case in 1887. Albarran first used the cystoscope in a case in 1897. Of the twenty-two cases reported, cystoscopic examination has been made in twelve and a renal functional test in only four. The remaining cases were accidentally discovered at operation or at autopsy.

The case which the author wishes to report is unique for two reasons: first the patient is the youngest to have recovered, and, secondly, she was relieved by the simplest type of operative procedure yet applied.

CASE REPORT

J. R., a child of six years, had always had incontinence of urine day and night. She voided normally at each urination during the day about 200 c.c. of clear urine. She had always worn diapers and her parents had applied various methods to effect a control of the urine without avail. The child, herself, was beginning to show shyness at school because of her misfortune. Her past history contained an attack of pyelitis when she was one year old. Her family history was irrelevant.

Examination showed a well developed, although rather delicate, healthy child. The head, chest, abdomen and external genitalia were

normal. The urethra was normal but clear urine was seen to ooze slowly from the vagina. The kidneys were palpable at their lower poles but did not appear enlarged or tender. Rectal examination disclosed normal pelvic organs. All reflexes were considered within normal limits.

Laboratory Findings: The red blood count was 4.5 million with 83 per cent hemoglobin, 6,600 white blood cells and a normal differ-

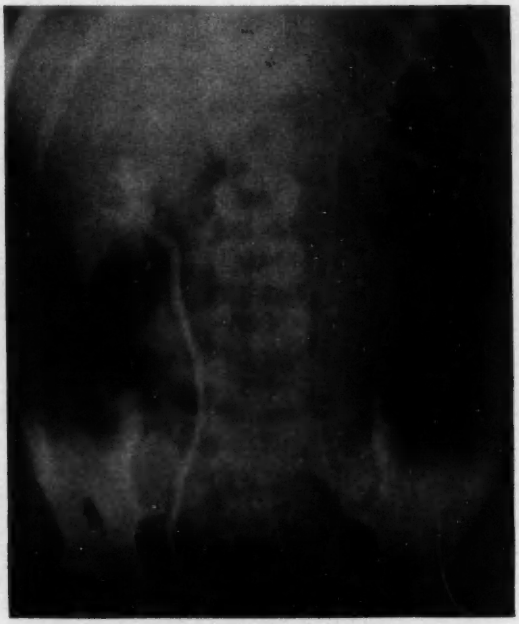


Fig. 1. Retrograde pyelograms showing normal left kidney and ureter and right kidney pelvis rotated on its vertical axis.

ential and smear. The bladder urine was clear, acid, specific gravity 1.016, albumin 0, sugar 0, without casts, pus cells and organisms. The vaginal urine was clear, specific gravity 1.004, with a rare white blood cell and no organisms. The phenolsulphonephthalein test was 70 per cent the first hour and 7.5 per cent the second hour. None was obtained from the vagina. The Kahn test was negative.

Cystoscopy was done under nitrous oxide anesthesia after dilating the urethra. The bladder capacity was 200 c.c. The mucous mem-

brane was free from inflammation, tumors, stones and diverticula. The ureteral orifices appeared normal as well as did the trigone and vesical neck. Both ureters functioned clear urine. They were readily catheterized with No. 4 olive tip catheters. An intravenous phenolsulphonephthalein test was given which appeared in five minutes on the left and six minutes on the right, with 18 per cent from the left and 15 per cent on the right in thirty minutes. Just a faint trace was obtained from the vagina at this time. The urines from the bladder and both ureters were normal and free from infection. Bilateral urograms disclosed normal kidney pelves, calices and ureters with rotation of the right kidney on its vertical axis. Additional findings were six lumbar vertebræ and a spina bifida of the first sacral segment (Fig. 1). A cystogram was done and found to be within normal limits. Acriflavine was introduced into the bladder, but none escaped through the vaginal os. At a second cystoscopic examination indigo carmine was given intravenously. A heavy color was obtained within a few minutes from each kidney; but only a faint trace at the end of thirty minutes was noted from the vagina. An intravenous skiodan series was executed which did not give any additional information in regard to renal shadows nor were there any evidences of a third pelvis. A vaginal cystoscopy and endoscopy disclosed urine to "well-up" from the sulcus between the anterior lip of the cervix and the vaginal vault, but the exact opening could not be visualized or catheterized.

The author concluded that the child had a third ureter which emptied into the upper vagina, but the information as to which side it might belong could not be ascertained.

Operation was performed October 18, 1933. Under nitrous oxide and ethylene anesthesia the abdomen was opened in the midline above the pubis after both ureters had been catheterized. A tubular cystic mass the size of a finger had its lower origin in the right broad ligament and ran upward toward the right kidney ventral to the ureter which contained the catheter. The main portion of the supernumerary ureter protruded into the peritoneal cavity as if by a mesentery. Mercurochrome injected into the lower segment of the large ureter escaped from the vagina. The ureter was then followed down to the cervical neck where it became quite small. Here it was cut and ligated. This abdominal wound was closed and a second incision made in the upper right quadrant to expose the kidney and ureter, transperitoneally. The large ureter ran to the upper pole of the kidney where a moderately dilated pelvis was noted. The blood supply was so intricate, and there not being any sharp dividing line between the normal kidney and the upper one, that it was thought best to do a ureterectomy (Fig. 2). The upper pelvis was firmly ligated with No. 000 chromic catgut and the ureter removed *in toto*. This was considered safe because the urine from the ureter was determined to be free from infection. The left ureter was found to be normal. This in-

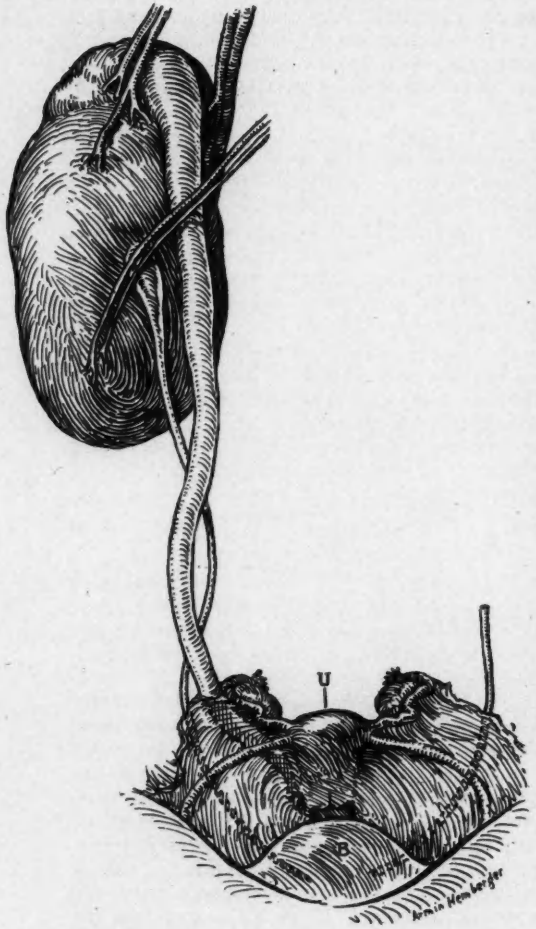


Fig. 2. Schematic drawing of right kidney with supernumerary ectopic vaginal ureter. U = Uterus; B = Bladder.

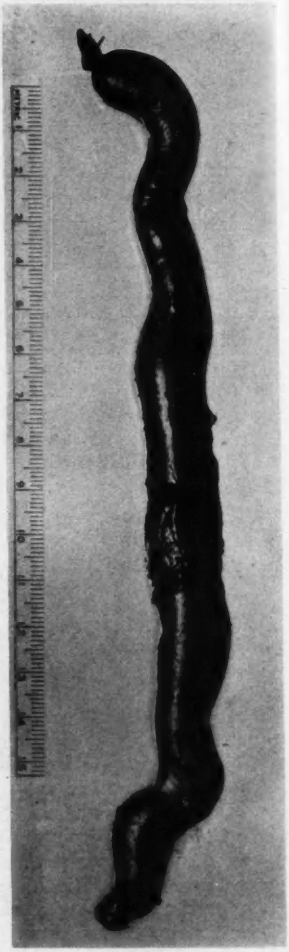


Fig. 3. Photograph of ectopic vaginal ureter, right.

cision also was sutured without drainage. The ureter removed was 1.5 cm. in diameter and 21.6 cm. long (Fig. 3).

REPORTED CASES

1. *Albarran.*—The patient, twenty years of age, complained of dripping urine in addition to normal urinations. The urine was found to escape from a small fistula from the anterior vaginal wall. Cystoscopic findings showed a normal bladder and two normal ureteral openings. The fistula on the anterior wall of the vagina was 3 cm. from the os and was probed for 20 cm., thereby proving that it did not join either ureter or the bladder. The auxiliary ureter was ligated and implanted into the dorsal bladder wall. The bladder and vaginal wounds were closed. *Operation* was unsuccessful, so the large vaginal fistula which did not communicate with the bladder was closed with the "lappen spalteung principle." Complete recovery.

2. *Alsberg.*—The patient, eighteen years old, had had incontinence from birth. She also voided normally. On the front wall of the vagina was a fistulated vesicle which was regarded as a wolffian duct. This was extirpated as far up as the parametrium on the right; but the patient died on the twenty-third day of pyemia. Autopsy showed that the "vesicle" reached to the right kidney pelvis and was therefore a ureter. On the left side there were two normal ureters terminating normally in the bladder.

3. *Connitzer.*—This case is that of an autopsy with bilateral double ureters on the left side. Both ureters emptied into the bladder. On the right side, a ureter ran from the upper kidney and terminated into the vagina by a vaginal cyst. The patient apparently died of pyelitis.

4. *Davenport.*—A woman, twenty-nine years of age, the mother of three children, had had incontinence of urine from the vagina and normal urinations all her life. The dripping from the vagina varied at intervals. She had noticed some thickening of the anterior vaginal wall with a projection for about 2 inches of tissue. On the papilla-like mound of this projection, there seemed to be an opening for the escape of urine. *Operation:* The ureter was separated from the front wall of the vagina and inserted into the bladder. A second operation closed the fistula. *Result:* Recovery.

5. *Depaul.*—Autopsy—exstrophy of the bladder revealed two completely separate uteri and vaginæ with atresia ani. The right ureter emptied into the right vagina by an enlarged opening running along the lateral wall of the uterus. The left kidney was one-third smaller than the right and was located in the depths of the pelvis. The ureter from this kidney also ran along the wall of the uterus and communicated with the vagina by a small opening.

REPORTED CASES OF ECTOPIC VAGINAL URETERS

No.	Reported By	Age	Main Symptoms	Opening	Side	Inf.	Cystoscopy	X-ray	Operations	Result
1	Albarran 1897	20	Vag. dripping. N. U.	Ant. vag. wall.			Normal bladder		1—Attempt implantation into bladder. 2—Implantation into base of bladder.	Recovery
2	Alsberg 1895	18	Vag. dripping. N. U.	Ant. vag. wall as a vesicle.	R	+			Extirpation of lower ureter.	Died 23rd day of pyemia. Autopsy showed normal bl.
3	Connitzer 1895		Vag. dripping. N. U.	Ant. vag. wall as a cyst.	R	+				Autopsy. Died pyelitis.
4	Davenport 1890	29	Vag. dripping. N. U.	Ant. vag. wall projection.					1—Separation lower ureter from vaginal wall. 2—Implantation into bladder.	Recovery
5	Depaul	Newborn	Exstrophy bladder.	2 vaginæ	L					Autopsy
6	Emmett 1887	30	Vag. incontinence. N. U.	Small opening near cervix.					1—Ureter dissected out. 2—Implanted into bladder.	Died of pneumonia
7	Herbst and Polkey 1927	12	Vag. incontinence. N. U.	Ant. vag. wall 1.5 cm. in front of cervix.	R	0	Normal bladder	+	Heminephrectomy.	Recovery
8	Israel 1918	32	Purulent vag. discharge. N. U.	Not located	L	+	Normal bladder	+	1—Pyonephrosis drained. 2—Nephrectomy.	Recovery
9	Kallmann 1923	21	Pain right side. Vag. urine. N. U.	Not located	R	+			1—Operation for appendicitis. 2—Pyonephrosis drained. 3—Nephrectomy both rt. kid.	Recovery
10	Katz	25	Incontinence since birth.	Ant. wall near hymen.	R		Accessory ureter, L.		Neocystostomy, right.	Recovery
11	Katz	23	Incontinence	Ant. wall near hymen.	R		Absent R ureter. Normal L. ureter.	+	None.	Spontaneous cure after five months.

				near hymen.			R ureter. Normal L. ureter.			cure after five months.
12	Kelley 1931	19	Incontinence. N. U.	Ant. vag. wall 3 cm. from cervix.	L	0	Normal bladder only R. ureter.	+	Left nephrectomy.	Cured
13	Knoepfelmacher	4	Pussy from vag. Large mass in left flank. N. U.	Not located	L	Strep.			Mass aspirated.	Died Autopsy
14	Kümmel and Graff 1913	15	Dripping from vag. N. U.	Not given	R and L		Normal bladder		Rt. pelves anastomosed; lt. ureter (upper) brought to skin.	Recovery with left sinus.
15	Linck 1904	7	Vag. urine N. U.	Not located	R	+			1—Operation for appendicitis. 2—Excision both rt. kidneys.	Recovery
16	Milton 1893	30	Vag. dripping. N. U.	Ant. wall 1.5 cm. from os.	R	+			Rt. ureter inserted into base of bladder.	Recovery after much pain in kidney.
17	O'Conor 1930	38	Partially incontinent.	Lat. to cervix L.	L	0	Normal bladder only R. ureter.	+	Ureter transplanted into bowel.	Reported well after seven years.
18	Ottow 1930	32	Incontinence since birth	Ant. vag. wall.	R and L	+	Normal bladder	+	1st—neocystostomy, right. 2nd—accessory, left kidney removed.	Satisfactory
19	Palfin	Foetus		2 vaginæ lt. ureter lt. vagina	L					Autopsy
20	Samuels et al. 1922	29	Vag. urine N. U.	7 mm. in front of cervix on ant. wall	R	0	Normal bladder	+	Heminephrectomy.	Recovery
21	Sargent 1930	23	Incontinent and N. U.	R. Lat. wall half way to cervix.	R		Two L. ureters one R. ureter.	+	Two unsuccessful attempts to ligate lower end of ureter, third operation neocystotomy.	Clear urine after four months.
22	Walz 1931	23	Incontinence	Ant. wall 1.5 cm. from hymen.	R	+	Normal bladder	+	Complete right nephrectomy.	Cured
23	Deming 1934	6	Vag. urine N. U.	Ant. wall near cervix.	R	0	Normal bladder	+	Right ureterectomy.	Recovery

Vag. = Vaginal. N. U. = Normal Urination. Ant. = Anterior. Inf. = Infection. Bl. = Bladder.

6. *Emmett.*—A thirty-year-old single woman had incontinence of urine with normal urinations. The ureter was found to terminate in the upper part of the vaginal wall near the neck of the uterus. *Operation:* A portion of the ureter was dissected out and implanted into the bladder in its normal position. *Result:* Ureteral incontinence. Ureteroplastic operation was done and was followed by pneumonia and death.

7. *Herbst and Polkey.*—The patient, twelve years of age, had always had dribbling of urine day and night from the vagina and normal urinations. Vaginal examination showed the opening of the vaginal ureter 1.5 cm. in front of the cervix in the midline on the anterior wall. Cystoscopy disclosed a normal bladder with normal right and left ureters. Urograms were given as normal. The right kidney was somewhat larger and lower than the left but showed a slightly smaller pelvis. The superior calix was broad and pushed downward. The upper right pelvis was long and narrow and was connected with the vaginal ureter. The urines were free from infection from all three ureters. Functional test was not done, but the diagnosis was correctly made. The supernumerary ureter was moderately dilated above the lower end. *Operation:* Heminephrectomy and partial ureterectomy were done. The supernumerary kidney having its own blood supply was removed without disturbing the lower kidney. *Result:* Cured.

8. *Israel.*—A patient, thirty-two years of age, complained of pain in the left kidney region, frequency of urination and purulent vaginal discharge. Swelling about the size of the fist developed in the left flank. A diagnosis of suppurative pyelonephritis was made. The abscess was opened and was found to lie, not around the kidney but inside the organ. It was drained. The vaginal discharge stopped. After the wound healed, the vaginal discharge began again. The patient had several recurrent attacks. X-ray showed that the organ was the third kidney. Insertion of the ureter from the third kidney was thought to be the vagina, but its point was not definitely located. The upper kidney on the left was removed with its ureter. Recovery of the patient was slow. Histologically, the ureteral wall was found to contain normal circular and longitudinal muscular layers, but the epithelium and subepithelium layers contained numerous round cells. The adventitia and connective tissue were very much thickened and fibrous.

9. *Kallmann.*—The patient, twenty-one years of age, had had a sudden attack of pain in the right lower quadrant. There were no gastro-intestinal symptoms. The abdomen was distended. The liver, spleen and kidneys were found to be normal. Vaginal examination was painless. The ileocecal region showed definite resistance and was sensitive to pressure. The patient was operated upon for appendicitis, but the appendix was found to be normal. The pain became gradually stronger in the region of the right kidney. The urine from the blad-

der, which had formerly been clear, now became purulent, as was also that from the vagina. The "subphrenic or retrocecal" abscess was opened. The patient's temperature dropped, but there was a persistent lumbo-urinary fistula which necessitated a second operation. The fistula was found to have been due to a kidney whose upper part was pyonephrotic. The urine filled this sac, from which escaped an accessory ureter which was also filled with pus. The exact location of the termination of the ureter was not found, although there was not any doubt that it terminated in the vagina. The kidney was removed. The surgical specimen showed two ureters, one of which was greatly enlarged, leading to the upper portion.

10. *H. Katz.*—A young woman of twenty-five years had had incontinence since early youth. The vaginal ureter was found to have an opening on the anterior wall near the hymen. Operation disclosed bilateral ureters with the ectopic vaginal ureter on the right. The accessory ureter was implanted into the vertex of the bladder with complete recovery.

11. *H. Katz.*—A single woman of twenty-three years had always had incontinence of urine. Examination disclosed an opening of a vaginal ureter at the seam of the hymen on the anterior vaginal wall. X-ray showed screw-shaped supernumerary ureter on the right with a normal ureter and kidney pelvis on the left. Operation was refused by the patient. After five months of gradual diminution in the incontinence, it ceased. The spontaneous closure is explained on the basis of occlusion of the ureter after injection of x-ray medium. No pain was experienced in the right kidney region.

12. *Kelley.*—A girl of nineteen years had always had incontinence of urine, but had voided normally. Examination showed a normal, well developed individual. Clear fluid escaped from between the labia. Cystoscopy showed a normal bladder with only the right ureteral orifice. Indigocarmine given intravenously escaped from the right ureteral catheter and from the vagina. The source of the vaginal urine was found to be from a small orifice on the anterior vaginal wall 3 cm. from the vaginal orifice. A No. 5 catheter was passed for 12 inches. A pyelogram suggested an infantile left kidney. Urines were normal from both kidneys. Phthalein test showed 35 per cent in twenty minutes with three minutes appearance time on the right and 1.5 per cent in the same time with an appearance time of three minutes from the left. A left nephrectomy was done. The kidney showed little functioning tissue, measured 5.5x2.6x1 cm. and weighed 11.5 grams. The ureter was small. The microscopic examination of the kidney disclosed architecture of infantile type. Recovery of the patient was complete.

13. *Knoepfelmacher.*—A girl, four years of age, had pain and swelling of the left side. She voided normally and also passed cloudy

urine from the vagina. Catheterized specimen of urine from the bladder was clear and showed no albumin. There was moderate anemia, enlarged liver and spleen. Below the latter was an elastic resistant area which could be separated from the spleen.

Rectal examination revealed no evidence of tumor. The mass was punctured from the back. Purulent urine with streptococcus was obtained. Pressure upon the vagina from the rectum caused pus to escape from the vagina. Pressure upon the tumor did not cause pus and urine to escape from the vagina. *Clinical diagnosis* was retroperitoneal abscess with fistula into the vagina. Since the urine was clear it was thought that the kidney could not be the origin of the abscess, and since the bones were normal the retroperitoneal lymph glands were taken as the origin of the abscess. Autopsy showed the left kidney divided in two; the upper half was thoroughly abscessed with a pelvis of its own. It was enlarged, filled with pus and communicated with the vagina by means of a distorted and enlarged ureter. The lower half of the kidney was free from abscess and from its pelvis there was a normal ureter leading to the bladder. The right kidney also had a double pelvis with two separate ureters which crossed and ended in the right side of the bladder. The liver was amyloid in type. The exact point of the lower end of the ureter emptying into the vagina was not determined.

14. *Kümmell and Graff.*—The patient, fifteen years of age, had four ureters, and had constant dripping of urine from the vagina in addition to normal urinations. Cystoscopy showed a normal bladder with normal ureter emptying on each side. Examination of the vagina showed a right accessory ureter which was probed without difficulty. The left was probed with some difficulty. The right kidney was exposed and the pelves anastomosed. This was difficult, due to the small size of the patient. The left ureter was separated at a later operation, tied off and brought to the skin. The patient completely recovered with a draining sinus on the left.

15. *Linck.*—The patient, aged seven years, had an attack of pain on the right side which was thought to have been due to appendicitis. At operation a double right kidney was found. The upper kidney was drained and found to contain pus. It drained off and on for some time with a development of an extensive fistula as well as a purulent drainage from the vagina. Complete extirpation of both kidneys on the right was done, with recovery. The exact location of the termination of the ureter within the vagina was not definite.

16. *Milton.*—The patient, aged thirty years, had always had dripping of urine from the vagina and voided normally. She was married at the age of thirteen. An opening on the anterior vaginal wall 0.5 inch from the os was found. This was probed in the direction of

the right kidney. It functioned 2 ounces of urine per day. There was no mention of infection. *Operation:* The right ureter was inserted into the base of the bladder. Convalescence was followed by much pain in the region of the right kidney for a long time, but eventually the patient was cured.

17. *O'Conor.*—A woman of thirty-eight years had always been partially incontinent. She had had gonorrhea and a bilateral salpingectomy six years before. Cystoscopy showed only the right ureteral opening. Vaginal examination showed urine escaping from an orifice above and lateral to the cervix. This was catheterized and clear urine obtained. Indigocarmine output was good. Pyelograms showed normal left ureter, calices and pelvis. The ureter was transplanted into the bowel with recovery. Seven years later, she was reported to be well and no urologic study was made.

18. *Ottow.*—A nullipara of thirty-two, who had complained of incontinence since childhood, was found to have a small opening on the anterior vaginal wall which put out urine, but which was too small to allow the entry of the smallest catheter or probe. X-rays showed a double kidney pelvis on the right with two ureters and a single upper urinary tract on the left. A laparotomy was done and the lower ureter on the right implanted into the bladder after the Fritsch-Stoeckel method. Incontinence continued. A second laparotomy was done and an accessory left ureter was found emptying into the vagina and leading to a cherry sized kidney above the normal left kidney, but receiving its blood supply from the main kidney. The accessory kidney and ureter were removed. The result was satisfactory. Histologic examination showed the left ureter, which was dilated, to be normal, while the rudimentary kidney showed few normal glomeruli and tubules with some fibrosis calcified area and colloid deposits in distended tubules. No sphincter was found at the lower end of the ureter, which accounts for some evidence of infection in the kidney. (Case of bilateral accessory ureters emptying into the vagina.)

19. *Palfin.*—Autopsy report of an infant that had two uteri and two vaginæ. The left ureter was inserted into the left vagina; the right vagina into the left intestine.

20. *Samuels, Kern and Sachs.*—The patient, single, twenty-nine years of age, complained of incontinence. She voided normally but has had day and night urinary leakage from the vagina since birth. At six she was operated on for vesico-vaginal fistula without success. Menstruation was normal. Vaginal examination showed opening of the right ureter in the anterior wall of the vagina 7 mm. in front of the cervix. Cystoscopy showed a normal bladder with normal right and left ureteral openings. The urine from each of the bladder ureters

ran three times as fast as that from the vaginal ureter. The urine from all three ureters was sterile. The phthalein functional test showed right kidney 30 per cent, left 42 per cent, and vagina 2.5 per cent X-rays showed normal right kidney pelvis and a supernumerary hydro-ureter. They concluded that the hydo-ureter was the result of the plastic operation. The operation disclosed a supernumerary upper right kidney which was removed as it had separate vessels from the main kidney. The supernumerary kidney was 4x4 cm. The ureter and blood vessels of the upper kidney passed posteriorly to the vessels of the normal kidney. Microscopically, the kidney removed showed perfect pyramids which were dwarfed. The ureteral walls were thickened. Recovery.

21. *Sargent.*—A working girl of twenty-three had had urinary incontinence since birth and also had normal urinations. She had never had any serious illness. Examination showed a normal physical condition except for hypertrophy of the labia minora and clear fluid escaping from the vagina. Vaginal examination showed a mucous ridge running on the right vaginal wall and half way back was seen a small opening from which clear urine escaped. This was catheterized for a distance of 2.5 cm. Cystoscopy done at the same time disclosed a normal bladder except for two ureteral openings on the left. All four catheters were injected. The vaginal ectopic ureter ran to the upper right kidney. Phthalein escaped through the vaginal ureter, but the amount was not determined. Fifty per cent was obtained from the other three catheters in thirty minutes. X-ray suggested that the upper right kidney was rudimentary. Two attempts were made to ligate the vaginal end of the ureter without success. A third operation was successful, transplanting the lower end of the ureter into the base of the bladder. Although the patient had some febrile reaction, a cystoscopy four months later showed an apparently clear urine.

22. *Werner Walz.*—A twenty-three year old virgin was noted to have incontinence of urine since childhood. By means of a Hinzelmann colposcope a small slit-like opening was found on the anterior wall 1.5 cm. from the os hymen and slightly to the right of the midline, from which escaped at intervals small drops of fluid. This was catheterized for a distance of 24 cm. X-rays and cystoscopy revealed an accessory ureter on the right which was dilated and led to a hydronephrotic upper kidney. The left kidney and ureter were normal. There was very little function from the accessory kidney, which was infected with B. coli. At operation a complete right nephrectomy was done because the upper hydronephrotic kidney was not sharply defined from the lower normal kidney. Convalescence was complete. Microscopic study of the kidney showed evidence of inflammation.

23. *Deming.*—See author's case reported herein.

DISCUSSION

Embryology.—The explanation for a supernumerary ectopic vaginal ureter has several theories, the most logical of which is based on the fact that instead of a single invagination from the wolffian duct there are two or more anlagen, each forming a ureter with separate implantation into the kidney. As the wolffian duct shifts with the urogenital sinus downward, it carries the upper ureter with it and causes a lower implantation of the upper ureter. If the two ureteral buds develop at the same time they may be found with their openings near together in the bladder; but if the upper ureter develops later, it may be carried below the bladder by the Mullerian duct to empty into the genital tract as in the vagina.

The vaginal opening for these ectopic ureters is practically always on the anterior wall in the midline, although as the opening nears the cervix it may become more lateral. Three are described as pinpoint openings on ballooned cyst-like masses. Usually these are single openings, although one is described with several openings. Three were found near the cervix. Five were not definitely located.

Incidence.—The age incidence shows two at birth with various other anomalies of the genito-urinary tracts, three more in the first decade, four in the second, five in the third, one in the fourth; the age of one was not given. The right ureter was involved in 54 per cent of the cases while the left was involved in 25 per cent and bilateral ectopic condition was found in 18 per cent. The side was not mentioned in three reports. In twelve cases the vaginal ectopic ureter was supernumerary on the side involved. In three cases the ectopic ureter was the single ureter while on the opposite side a supernumerary ureter emptied into the bladder. The above percentages are probably not exact as cystoscopy was not performed in all cases and the data are insufficient; but it is quite apparent that the right side is the more frequently involved and that bilateral ectopic ureteral openings occur in about one-fifth of the cases. The Weigert-Meyer theory always holds good; for the vaginal supernumerary ureter always runs to the upper kidney.

Pathology.—The pathology of the kidney and ureter connected with the ectopic vaginal ureter has never been appreciated. Only four specimens are described in detail. Grossly at operation most of them have been found to be thin walled sacs with dilated pelves

and ureters. In the microscopic study of the two uninfected kidneys the renal tissue was hypoplastic. The ureters are enlarged, with normal histologic pictures. Whether normal valves exist at the lower end is not as yet determined, although most cases are described as being constricted at this area. The function from these kidneys is insignificant by the phenolsulphonephthalein, methylene blue and indigocarmin tests. The specific gravity of the urine was very low in the author's case. It would seem, from the clinical and pathologic studies, that these supernumerary kidneys do not, as a rule, contain much renal tissue and are very prone to infection which may develop into a large pyonephrosis or spread to the lower kidney.

Symptoms.—The symptoms of ectopic vaginal ureter are quite definite. All cases had vaginal dripping of urine day and night. The amount of urine varied somewhat and often was increased when the patient became excited. In addition, normal urinations occurred. When the ectopic ureters became infected, purulent urine passed the vagina as reported in two cases. In four cases the symptoms from infection such as pain and elevation of temperature overshadowed the urinary picture to such an extent that the patients were operated upon for appendicitis or renal suppuration. Without infection, the patient does not complain of any discomfort within the kidney region. The continued incontinence causes shyness and seclusiveness as well as nervous irritability.

Diagnosis.—Diagnosis of ectopic vaginal ureter should not be difficult, as all cases gave a history of vaginal dripping of urine since birth, together with normal urinations. Careful local examination as to the source of the urine, whether it comes from the vaginal os or from around the urethra, demands only the acuity of ordinary vision. Too often it is taken for granted that the urine escapes from the urethra. As to the location of the opening of the ureter within the vagina, more difficulty may be encountered. Especially is this true in the child where the canal is small. Any insertion of an instrument for vision often causes enough pressure to stop function. Again, urinary flow from these ureters is slow and intermittent and they fail to excrete much of any dye that may be injected. Where there is a vesicle or cystic pouch leaking urine, the exact location may be more readily suspected. However, prac-

tically all empty near the midline somewhere on the anterior vaginal wall. In the twelve cystoscopies recorded, all reported normal bladders with normal ureteral openings. In only six cases was the ectopic ureter catheterized and a pyelogram made. One might expect that an intravenous skiodan injection would be of value, but owing to the diminished function of these kidneys the secretion may be very slow and inadequate in amount to show an outline of the pelvis. This was attempted twice in the author's case, but shadows other than those of the normal kidneys could be interpreted in retrospect only. Plain x-rays of the kidneys are apparently not to be relied upon as the upper pole of the kidney lies high, and definite outlines are not obtained unless some means like perirenal air injection be made. The possibility of a vesico-vaginal fistula was ruled out by the usual method in the more recent cases. So far, a diagnosis of bilateral ectopic vaginal ureters has not been made preoperatively. With the available equipment all cases should be diagnosed in childhood.

Treatment.—There was an attempt by the earliest writers to conserve the kidney and ureter. Five patients in the early cases received implantation of the ureter into the base of the bladder with two deaths from infection, and a third finally recovered after a prolonged illness undoubtedly due to a renal infection. The two patients who recovered from such operative procedures required two operations each and there is no follow-up to indicate the final result. Nephrectomies were done with recoveries in those cases where extensive suppuration occurred. Two badly infected patients, not treated surgically, died from the suppurative process. Heminephrectomy was accomplished by Herbst and Samuels. The kidneys in their cases were not infected and were more or less distinct, with separate blood vessels. Kümmell and Graff report anastomosing the pelves successfully on one side. O'Conor transplanted one into the bowel.

Before any surgical procedure is applied it should be borne in mind (1) that these kidneys have but little functional value, (2) that the ureter is most always dilated and (3) that these kidneys have a tendency to become infected. Neocystotomy precludes infection. Once infection has taken place a complete nephrectomy is indicated, provided there is an opposite kidney. If the supernumerary kidney remains free from infection, disposal of the super-

numerary kidney and ureter should be brought about by surgery or process of atrophy. Where dilatation has not taken place in the pelvis and ureter the pelvic anastomosis of Kümmell and Graff seems feasible. Where the supernumerary kidney and ureter are dilated and the kidney possesses distinct and separate vessels, a heminephrectomy is the procedure of choice. But many of the supernumerary kidneys showed a very intricate blood supply and a heminephrectomy could not be done without interference with the vessels of the good kidney. Such was the condition found in the author's case. Here a ureterectomy seemed to be the operation of choice. It was easy to accomplish and a complete conservation of the good kidney was maintained. The supernumerary kidney apparently atrophies as one would not expect any more complication than ligating a normal ureter. To leave a large cystic ureter in place would offer chance for infection. While ureterectomy has not been corroborated it is justifiable in children and in cases diagnosed before infection has taken place.

CONCLUSIONS

1. Ectopic vaginal ureters produce uniform symptoms of vaginal dripping of urine together with normal urinations.
2. The opening for ectopic vaginal ureter is on the anterior vaginal wall near the midline anywhere from the hymen to the cervix.
3. The supernumerary ectopic vaginal ureter always runs to the upper pole of the kidney.
4. The right side is the more frequently involved.
5. The kidney attached to the ectopic vaginal ureter is of little functional value and is prone to infection.
6. Diagnosis should be made in the first decade.
7. Intravenous skiodan may not be of value in diagnosis of these cases.
8. No attempt should be made to conserve these ureters and kidneys.
9. Heminephrectomy may be done if vessels are distinct to each kidney.
10. Once infected, nephrectomy is indicated.
11. Total ureterectomy offers an easy method of treatment when infection has not taken place.

BIBLIOGRAPHY

1. ALBARRAN: Uretère surnuméraire ouvert dans la vulva et dans le vagin. Gaz. d. hop., 70:743, 1897.
2. ALSBERG: Reported in discussion of Wolfler's case. Zentralbl. f. Chir., 22:118, 1895.
3. CONNITZER: Fall von beiderseitiger Verdoppelung des Ureteren. Zentralbl. f. Gynaek., 19:266, 1895.
4. DAVENPORT, F. H.: A Case of incontinence of urine due to malposition of the ureter. Trans. Am. Gynec. Soc., 15:343, 1890.
5. DEPAUL: Mémoires de la Soc. de Biol., 1852 (d'après Delmas).
6. EMMETT: Pratique des Maladies des femmes, 1887.
7. HERBST, R. H., and POLKEY, H. J.: Ectopic ureteral openings. Report of a case. Jour. Urol., 17:61, 1927.
8. ISRAEL, I.: Diagnose und Operation einer ueberzaehligen pyonephrotischen Niere. Berl. Klin. Wchnschr., 55:1081, 1918.
9. KALLMANN, D.: Ein Fall von Pyonephrose durch Ureter-Verschlufs bei zweiteiliger Niere; ein Beitrag zur Klinik der ueberzaehligen Ureteren. Arch. f. Klin. Chir., 127:458, 1923.
10. KATZ, H.: Beiträge zur Kenntnis der ueberzaehligen ausserhalb der Blase mundenden Harnleiter. Zentralbl. f. Gynäk., 55:1536-1545.
11. KELLEY, S. B.: Report of a case of an ectopic ureter. Jour. Urol., 25:241-246, 1931.
12. KNOEPFELMACHER: Nieren-Ureteranomalie; Beiderseitiger Ureter duplex. Wein. Klin. Wchnschr., 11:297, 1902.
13. KÜMMELL, H., and GRAFF, H.: Garri-Kuettner Lexer. Handbuch der Chirurgie. 5th ed., 4:385.
14. LINCK, A.: Pyonephrose bei Verdoppelung der rechten Niere. Deutsche Ztschr. f. Chir., 75:51, 1904.
15. MILTON, H. M.: Persistent Gaertner's ducts treated in one case by diversion of opening from vagina to bladder. Lancet, p. 924, 1893.
16. O'CONOR, V. J.: Discussion. Jour. Urol., 23:376, 1930.
17. OTTOW, B.: Kritische Erwägungen zur Diagnose und Therapie der extravesikalen Harnleiterausmündung. Zentralbl. f. Gynäk, 54:3239-3259, (Dec. 20) 1930.
18. PALFIN: Reported by M. J. Delmas and P. Delmas: Annales des maladies des organes genito-urinaires, Paris 28, 1:984, 1910.
19. SAMUELS, KEARNS and SACHS: Supernumerary kidney with ureter opening into vagina. Surg., Gynec. and Obst., 35:599, 1922.
20. SARGENT, J. C.: Ureteral ectopia. Jour. Urol., 23:357-376, (March) 1930.
21. WALZ, W.: Zur Klinik der Enuresis Ureterica. Zentralbl. f. Gynäk., 55:2300-2305, 1931.

DISCUSSION

DR. THOMAS C. STELLWAGEN (Philadelphia, Pa.): I wish to present a simple method for the control of hermorrhage of the kidney both during and subsequent to operative procedures. Some of the members of the Association are conversant with the technic. It consists of a staff about 20 cm. long with a ring about 1.5 cm. in diameter placed at right angles to the long axis of the staff upon the end. The instrument resembles a vein stripper. The kidney is exposed in the usual way and the vascular pedicle identified and liberated from its attachments as far as possible. The ureter is also isolated. A flexible rubber tube of about the size of a No. 14 or No. 16 catheter is then passed about the vascular pedicle and brought out upon the back. The two free ends of the tubing encircling the pedicle are then laced through the ring upon the end of the staff. The tubing is gently pulled upon and the staff ring passed down the tubing. This automatically tightens the tubing about the pedicle and consequently restricts the circulation of the kidney. It acts in a capacity similar to the Esmarch band in amputations.

From time to time the tubing about the kidney pedicle may be loosened sufficiently to re-establish the circulation and so enable the operator to control bleeding points. You will find this technic facilitates operative surgery upon the substance of the kidney because of its practical control of hemorrhage. In the Jefferson Hospital we have used this method in five cases of heminephrectomy for double pelvis wherein we amputated the lower half of the kidney, which was the offending portion of the organ. These were done primarily because of calculus formation within the lower pelvis, which was poorly drained and infected. For a long time we have been impressed with the unreliability of catgut in the control of postoperative kidney hemorrhage. There may be some secretion from the kidney structure that has a very potent power for the solution of catgut that makes it unreliable. In three cases in the past we have had occasion to do a complete nephrectomy in individuals upon whom surgery had been done on the kidney. It became necessary to remove the kidney because of hemorrhage. The operation was in every sense an emergency. The kidneys were

examined and the catgut had all but disappeared from them. In one instance only the knots remained. One of these hemorrhages occurred fifteen hours after operation and the other two about two and a half days afterward. This instability of catgut led us to devise the method of control above suggested. After the operative procedures upon the kidney have been completed the rubber tubing about the pedicle is allowed to remain *in situ* with the ends projecting about 6 to 8 cms. upon the back. We are careful to see that there is no restriction permitted by the tubing about the pedicle. The wound is closed in such manner that there is ample room to pass the ring down along the tubing if necessary. The constriction ring instrument is kept sterile by the patient's bedside and the nurse and resident physician are instructed in its use. Should dangerous bleeding intervene, the ring is passed down the tubes and gentle tension made upon them in such manner that the hemorrhage will be controlled and the surgeon can take time to have the operating room prepared and do the nephrectomy under aseptic technic rather than use the old "poke in the dark" method by cutting the stitches and attempting to clamp the pedicle. The tubing acts as a drain and thus far has not been harmful. I wish to cite one case. This man was heminephrectomized and there was considerable oozing from the kidney stump, which was controlled by gauze packing. The packing was removed on the fourth day and a vicious hemorrhage ensued. This was readily controlled by the aforementioned device. The operating room was prepared for a nephrectomy. The constricting band was partially loosened after one hour and fifteen minutes and no bleeding ensued. The kidney was allowed to remain under constriction for another hour with more tension relieved and no bleeding and hence another hour of reprieve was tried. At the end of approximately the third hour there was no blood loss and we decided to wait. All tension on the device was taken off. This patient bled no more and the remaining half of the kidney was saved. It has since been checked and found to be secreting urine.

We believe that this device, because of its simplicity and its practical utility, will in a large measure eliminate the dangerous sequelæ from hemorrhage. This in turn we hope will warrant more conservatism in kidney surgery.

DR. JOHN H. CUNNINGHAM (Boston, Mass.): I want to show

a slide illustrating a case in which we got out of the difficulty of a sinus following ligation or injury to the ureter by a very simple method.

(Slide) This patient, a doctor's wife, had a hysterectomy for fibroids in May, 1929. Pain in the pelvis and left loin with temperature followed immediately, and on the fifth day there was a discharge of urine from the vagina. The patient was subjected to a great deal of study and the location of the sinus in the ureter was not established. She was referred to us in October, 1929. From May to October she was draining urine abundantly through the vagina, and little passed from the urethra. On more study, the details of which I will not take time to mention, we finally believed that the opening was high in the ureter near the inferior isthmus. Just what to do, of course, was a problem, but we thought perhaps it would be well first to put a ureter catheter up that ureter, which we did, and kept it there for four days, following which it was removed. There has been no leakage of urine since, a period of four years. I saw the patient on April 30 (1934), a few weeks ago, and she has remained absolutely dry ever since. I suggest, therefore, that the use of the ureter catheter is worth while trying before employing operative procedures.

Dr. Leon Herman (Philadelphia, Pa.): In connection with Dr. Sisk's paper, I would like to inquire whether members of the Association have ever encountered operative injury of the upper end of the ureter. Of course, practically all of these injuries involve the pelvic segment and the urologist's experience with ureteral injuries seems to be in direct ratio to the number of gynecologic friends he happens to have. The case that I wish to report was that of an operative injury of the abdominal ureter.

The patient was admitted for the treatment of hemorrhoids. A very diligent resident obtained a history of pain in the back and the x-ray disclosed a stone in the kidney. I was asked to study the man and found the case very suitable for posterior pyelolithotomy, which one of my friends did without any apparent trouble, and he afterwards said he hadn't even seen the ureter. The operation was simple, the kidney came up readily and a posterior pyelolithotomy was done without trouble. About six weeks later, I was asked to see the patient again, and found a urinary fistula. The study revealed a closed-off lower segment of the ureter, the end

having been turned outward and apparently buried in the lumbar fascia. It was quite closed. I told my friend he had in all probability ruptured the man's ureter.

We exposed the kidney and found that that was just what had happened. The ureter was completely torn across. The man had a perirenal abscess and a thoroughly disorganized kidney. We did a nephrectomy and the man recovered and left the hospital without his kidney, without his hemorrhoids and without any respect for the surgical profession.

DR. CHARLES M. MCKENNA (Chicago, Ill.): I enjoyed all three papers this morning, and want to talk particularly concerning Dr. Sisk's paper. I think his paper is most timely and brings out the value of intravenous urography in acute and traumatic lesions. It corresponds well with some work that we did about two years ago on this same subject. It will suffice to say that in dealing with a fistula or a suspected fistula of the genito-urinary tract, skiodan will usually clear up the diagnosis immediately. This was brought out very clearly by Dr. Sisk when he showed the transplant picture. All three papers were very practical, and can be utilized in everyday work.

DR. NATHANIEL P. RATHBUN (Brooklyn, N. Y.): I would like to say a word in discussion of Dr. Deming's paper. As you know, the diagnostic problems involved in some of these ectopic ureters are sometimes difficult. This may best be illustrated by a case that came under my care this winter. The patient, a female child of three, was admitted to the hospital with a typical attack of what seemed like acute pyelitis, high temperature and much pus in the urine. Following the subsidence of the acute symptoms, we made a cystoscopic examination and studied her. Much to our surprise we found no pus in the urine, no pus from either ureter, and pyelograms on both sides showed a normal condition, as we interpreted them. That was rather confusing. The voided specimens even then continued to show large amounts of pus.

We then made a cystogram. Our first cystogram apparently was a perfectly normal cystogram, and still the voided urines continued to show pus and the cystoscopic urines were absolutely free from pus and sterile. We looked in the urethra and could find no

opening of an ectopic ureter. The child was small and it was rather difficult to be sure we were not missing it, of course.

We then attempted to make a cysto-ureterogram, which was eminently successful and showed in addition to a picture of the bladder a huge sausage-shaped mass, apparently quite as much like a rectum as anything else, apparently going down to the rectum. On the strength of that we went ahead, assuming it was an ectopic ureter and bifid kidney, and did a heminephrectomy. Having completed the heminephrectomy, we were a little bit uncertain about the circulation of the remaining portion of the kidney and removed that also. Ten days later we operated again and removed both ureters, and we were able to demonstrate that the ectopic ureter emptied just at the sphincteric margin, the margin of the sphincter and the bladder.

DR. JOHN R. CAULK (St. Louis, Mo.): I would like to show a slide or two. I was particularly interested in Dr. Higgins' transuretero-ureteral anastomosis, and it turned out to give a very beautiful ultimate result.

There is one thing that occurs to me in the conduct of such an anastomosis and that is its effect upon ureteral stasis. I have observed in two cases of bifurcated ureters that at the union of the two segments there was no evidence of stricture, but the affected portion of the ureter revealed reverse peristalsis, the waves starting directly at the point of contact of the two ureters. It is my impression from these observations that the ureter which has the right of way interferes with the emptying of the other segment in all probability, not by the column of fluid or stricture, but by reverse peristalsis.

Some observers have doubted reverse peristalsis in the ureter, but there can be no question of its occurrence; I have observed it repeatedly both on the operating table and in following Dr. Gruber's experiments. I have seen reverse peristalsis produced by thermal, chemical, mechanical and pharmacologic means in the pig's ureter 108 hours after extirpation from the body. The practical point to be considered in anastomosing one ureter into the other in the manner which Dr. Higgins described is that there may be the possibility of obstruction in the manner mentioned.

Concerning ureteral injuries, I would like to cite the story of a case which occurred in my practice about a year ago in order to call

your attention to a technical procedure which was utilized in anastomosing the two ends of a severed ureter which differed tremendously in caliber. The patient had a uretero-abdominal fistula of three months' duration complicating a hysterectomy. The operation was done under spinal anesthesia. The upper ureter was found to be considerably dilated, at least 0.5 inch in diameter, and the lower segment, which had been imbedded in the scar in the pelvis, was of normal caliber. The ureter was freed above and below with ease so that the two ends could be overlapped at least an inch to obviate tension. The method employed in anastomosing these two ends was simply a tapering of the upper ureter by excising an inverted "V" wedge about 1 inch in length and suturing the lower end of the upper ureter, gradually funneling it down to its tip, which at this time was the same caliber at the lower end. The end-to-end union was splinted by a soft rubber catheter which was brought out of the ureter above the anastomosis, and the dilated ureter above was also drained by another large soft rubber catheter. Very few sutures were employed at the line of union, but several halliard sutures were employed to steady the splint away from the line of union.

As you can see by the pyelograms, at the end of the year there was a perfectly normal ureter, no sign of stricture at the anastomosis, and the functional capacity of the kidney is that of the other side.

In ureteral defects where certain amounts of the ureter have been destroyed (this has happened to me once during a diverticulectomy, in which instance 2 inches of ureter were accidentally removed), the problem of re-establishment of the canal is sometimes a serious one. In my case it was impossible to approximate the two ends; I therefore simply splinted the ureter over a soft rubber catheter and placed traction sutures between the two ends, leaving a vacancy of at least an inch. Within two weeks the ureteral lumen was established. I followed the patient for a number of years and there was always a patent ureter. Dr. Wiseman conducted a number of experiments on animals and found it was the universal tendency of the ureter to epithelialize around a soft rubber splint and re-establish its lumen, even if as much as a centimeter had been removed.

Concerning the most common ureteral injury, ureteral ligation,

I still believe, after twenty years of observation, that the simplest and safest procedure is to relieve tension and obstruction back of the ligation by renal drainage. I do not feel that deligation of the ureter is in any way comparable to it. In all the animal experiments which I conducted years ago, the ureter universally re-established its lumen. In the patients who have had nephrostomy following ureteral ligation, the end-results have always been excellent and there has been no mortality. I have watched a number of these women for years and, while it is impossible in several of them to pass a catheter up the ureter on account of tortuosity, ureteral emptying is perfect and renal function normal.

Dr. Clyde L. Deming (New Haven, Conn.): I wish to show some slides of experimental work on ureteral anastomosis. My associate, Dr. Neuswanger, and I have found that by tapering the cut end of the ureter into a long, slim process, tying a suture around this, and threading it onto a straight cutting needle, the needle with the ureter can be readily passed through the recipient ureteral wall into its lumen without an incision and downward for a distance of 2 or 3 cm., where it is held by supportive sutures of black silk. The slides show two such anastomoses at 3 and 8 cm. from the bladder. The first slide specimen was taken three months postoperatively and the second five months postoperatively. They do not show any dilatation of the ureters and the patency of both ureters is not in the least constricted. While this particular method has not been used clinically, I believe it has possibilities in conserving a ureter without infectious complications.

Dr. Ira R. Sisk (Madison, Wis.): I agree with our president's opinion regarding the value of nephrostomy in double ligation of the ureter. I have never had to deal with that situation but I believe nephrostomy is a better procedure than attempting to deligate the ureters through a fresh wound. Dr. McKenna's point regarding the distention of the bladder when re-implanting a ureter into the bladder is valuable.

Dr. Clyde L. Deming (New Haven, Conn.): I appreciate Dr. Stellwagen's discussion of my paper. The point I wished to make was that I didn't think it was necessary to do a heminephrectomy in the child where the urine was uninfected, thereby simplifying the surgical procedure.

EMPYEMA OF THE URETER ASSOCIATED WITH APLASIA OF THE KIDNEY

GEORGE GILBERT SMITH, M.D.

Boston, Massachusetts

The following case is sufficiently unusual to warrant its report.

S. G., male, a teacher forty-one years of age, was seen July 5, 1933. His only symptoms were a feeling of fatigue, one or two degrees elevation of temperature when he became tired, and an unpleasant odor to the urine. These symptoms first appeared six months before, after an attack which was thought to be grippe. No vesical symptoms had been noted; there had been no pain except an occasional dull ache in the back. Pus had been found in the urine.

Careful questioning brought no history of illness in childhood; the only previous illness had been a carbuncle of the left shoulder three years before. A physical examination showed the patient to be in excellent general condition, although he looked rather drawn. Neither kidney was palpable; prostate and external genitals were not remarkable. Cystoscopy, July 8, 1933, showed elevation of the trigone and bladder neck with a marked bas-fond. The bladder mucosa was generally reddened. The left ureter appeared normal, but no catheter could be passed more than 1 centimeter. The right ureter was not identified, but was thought to be represented by a depressed cavernous pocket in the right base. Six cubic centimeters of indigocarmin were injected into a vein, but practically no color appeared during the forty minutes of observation. His non-protein nitrogen was 34 milligrams per 100 cubic centimeters of blood; intravenous phenolsulphonephthalein showed a total of 50 per cent in two hours. The bladder residuum was 4 ounces. Inoculation of a guinea pig showed no tuberculosis. A flat radiograph of the abdomen was taken. The left kidney outline was faintly visualized. It appeared large. The right was not seen either before or after an intravenous pyelogram. No definite calculi were seen. No areas of calcification were visible in the region of either kidney. Intravenous pyelography showed that no dye was excreted by the right kidney even in the radiograph taken nearly two hours after injection. The left kidney excreted the dye rather slowly to fill an enormously dilated kidney pelvis and ureter. The calices were dilated but not so much as the kidney pelvis. The dilatation of the ureter extended down to the urinary bladder.

It was believed that the most important thing for the patient was to conserve the function of his left kidney. On July 12, 1933, a left nephrostomy was done. "A left oblique kidney incision was made, and

the kidney easily delivered. It appeared normal in size and appearance except for four or five firm, slightly elevated nodules about 0.5 c.c. in diameter on the cortex. One of these was excised for examination. The pelvis appeared slightly dilated and was incised. Ureteral catheters were then passed downwards and appeared to go into the bladder. The largest one passed was a No. 13 French Garceau catheter which went all the way without being gripped. A rubber tube was then

Fig. 1. Pyelogram of left kidney and ureter after nephrostomy.

drawn through the cortex from the pelvis outwards and the kidney replaced. The small incision in the pelvis was left open" (Fig. 1).

The patient made a good recovery from this operation, but continued to pass thick pus from his bladder. It was thought that in spite of the negative evidence of the x-rays he had a pyonephrosis of the right kidney. On July 26, 1933, exploration of the right renal area was done through a lumbar incision; no vestige of kidney was found. On

August 4, 1933, the patient was discharged from the hospital with his left nephrostomy working well.

On November 21, 1933, he again entered the Baker Memorial Hospital. He had gained weight and looked much better, but he still complained of feeling tired. He frequently had a slight fever. Cystoscopy

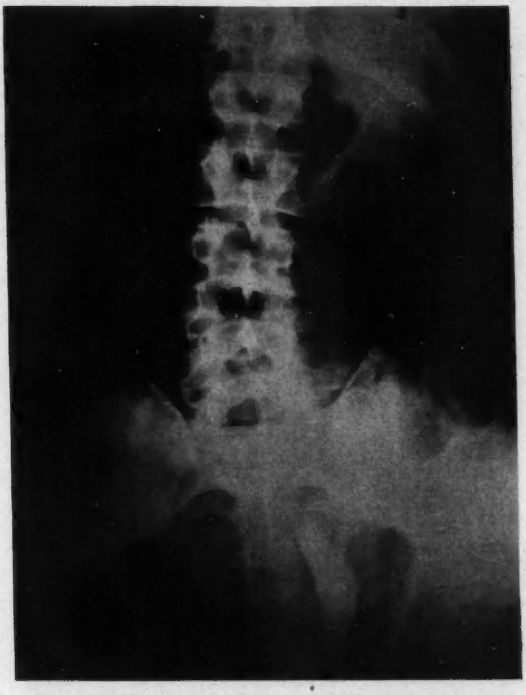


Fig. 2. Ureterogram showing dilatation of right ureter and extension of the ureteral pouch beneath the trigone.

(McCarthy cysto-urethroscope) showed nothing remarkable in the posterior urethra. The bladder appeared less inflamed than at previous examination. Upon withdrawing the cystoscope, a worm of pus was seen coming from the edge of the bladder neck on the right side. A catheter was passed into the orifice from which the pus came, and thick pus was obtained. Plain film and pyelograms were made (Fig. 2). These showed the radiographic catheter coiled in the urinary bladder

and pointed towards the right ureter. After injection, what appeared to be the right ureter was distended with iodide up to about the second segment of the sacrum, where it ended abruptly in a rounded smooth extremity. There were no shadows to suggest the outline of the right kidney, calices, or kidney pelvis. A small area of calcification was seen over the right side of the ilium which shifted considerably in its position and probably represented a tuberculous gland. It was not possible

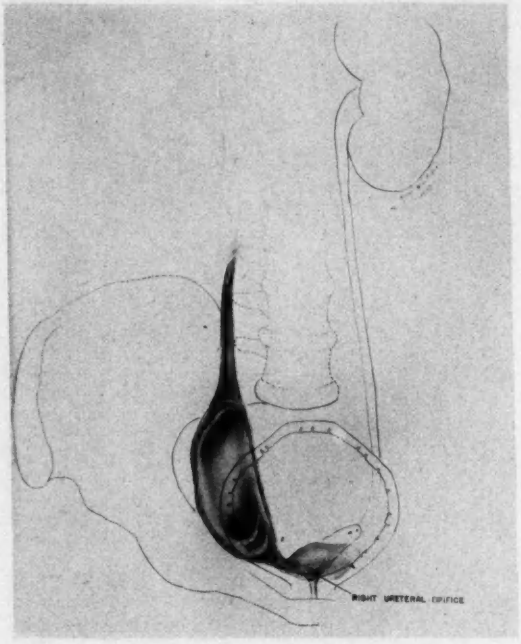


Fig. 3. Schematic drawing reconstructed from pyelogram and operative specimen, showing location of right ureteral orifice.

from this examination alone to make a diagnosis of pelvic kidney, but the absence of a kidney shadow in the right kidney area and the operative findings suggested that the kidney was low, probably in the region of the sacro-iliac joint. It is difficult to explain why this kidney pelvis, if present at all, did not fill with the medium.

On November 24, 1933, the patient was again operated upon and right ureterectomy was done. A median suprapubic incision was made.

The peritoneum was stripped off the right side of the pelvic wall. A dilated, thickened ureter was found intimately attached to the peritoneum. In freeing it the peritoneum was opened, but was sutured soon afterwards. The ureter was dilated up to the pelvic brim, where it began to narrow and extended as a fibrous cord for about 3 inches above the pelvic brim, ending apparently blindly in the posterior peritoneum. It was freed at the upper end and was dissected out down to its en-

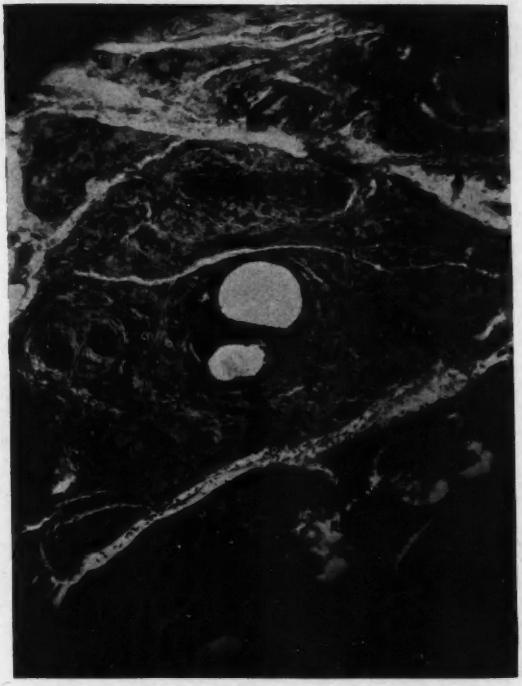


Fig. 4. Microphotograph of section from tissue about the upper end of right ureter.

trance into the bladder. For the terminal inch it was closely adherent to the bladder wall beneath the trigone so that the two cavities were separated by a thin, fibrous layer with mucous membrane on each side. The bladder over this area looked rather granular. The entire ureter was removed and the defect in the right lateral wall of the bladder was closed with a continuous suture of catgut. The bladder neck admitted

the tip of the finger easily. A tube was left in the bladder, cigarette wick in the prevesical space and a rubber drain in the right iliac fossa behind the peritoneum (Fig. 3).

The pathologic report stated: "The specimen consists of a section of ureter 22.5 centimeters long which has already been opened. The mid-portion forms a fusiform dilatation 11 centimeters in length with a circumference of 4 centimeters at its widest portion. The mucous surface is injected most intensely at its lower half. There are shaggy adhesions on its outer surface. The proximal end forms a fibrous cord 8 centimeters long in which a tiny lumen can be identified. In the distal end, which is 3.5 centimeters long, the lumen narrows immediately below the dilatation and then widens to a diameter of 1 centimeter. Diagnosis: Stenosis and atresia of the ureter. Pyoureteritis. Comment: In the fibrous cord at the proximal end there are scattered clusters of small gland tubules which may represent renal elements" (Fig. 4).

Convalescence was uneventful and the patient was discharged from the hospital on December 13, 1933. He returned to see me on February 6, 1934. As his doctor had been unable to make the nephrostomy tube drain, it had been left out. The fistula had closed promptly. The urine was absolutely clear; there was but 1 ounce residuum. The patient had gained 15 pounds in weight, had had no more fever, and felt very well. An intravenous pyelogram still showed a hydronephrosis and hydroureter on the left.

We have been unable to find in the literature the report of any case exactly comparable to this. Empyema of the ureter following nephrectomy is, of course, not uncommon. The case most nearly approximating ours is reported by Lau and Henline,[1] who found two ureters draining a double kidney on the right, and a third ureter, also on the right, which ended at the level of the fifth lumbar vertebra in a blind pouch. They stated that the "third ureter seems to end blindly or to pass to a possible aplastic, ectopic kidney."

The explanation of the dilatation and infection of the right ureter in our case is not clear. It is possible that an infantile kidney had been destroyed by infection, leaving only a few tubules to mark its location. Apparently the distention of the ureteral sac beneath the trigone caused the elevation of the trigone and the patient's inability to empty the bladder completely.

SUMMARY

A case is reported in which the right ureter terminated superiorly in a fibrous insertion in the peritoneum. In this fibrous

termination a few tubules were found. The lower end emptied into the bladder in an anomalous location; the entire pelvic ureter was dilated and full of pus. By pressure upon the trigone from behind, it had produced partial obstruction to the emptying of the bladder; the infection had caused a toxemia.

REFERENCE

1. Lau, F. T., and Henline, R. B.: Ureteral anomalies. Jour. Am. Med. Assn., 96:587-591, (Feb. 21) 1931.

URETERAL OCCLUSION FOLLOWING RADIUM IMPLANTATION INTO THE CERVIX

HENRY G. BUGBEE, M.D.

New York City

Since 1930, the writer has nephrectomized six patients at the Woman's Hospital, following irradiation of the cervix for carcinoma. During the past year, two other cases were referred to the urological department, one presenting an occlusion of both ureters, the other a unilateral occlusion; in both instances secondary to irradiation of the uterus.

Attention has been called by Dean[1] to injury of the urinary bladder following irradiation of the uterus, forty-seven instances of such injury being reported by him from the Memorial Hospital to 1933, but I have been unable to find any reference in the literature to involvement of the ureters subsequent to such treatment. One case of bilateral ureteral occlusion, following the use of the Percy cautery for cervical carcinoma, was seen by the writer in 1914, the patient having passed no urine for eleven days. Both ureters were transplanted into the dome of the bladder and the patient made a satisfactory recovery.

In the cases, which I herewith report, all patients, with one exception, were radiated at the Woman's Hospital.

CASE REPORTS

Case 1.—Mrs. M. C. was first admitted to the hospital October 7, 1921, at the age of twenty-four. Her father and a sister had died of pulmonary tuberculosis. Two and one-half years previously she had been operated on for a right tubal pregnancy, and three months previously she had attempted an abortion. On admission, a mass was found in the left vaginal fornix, and at operation a left salpingectomy was done for an unruptured tubal pregnancy. At this time, the blood, urine, and Wassermann examinations were negative. She was readmitted May 27, 1928, complaining of an irregular spotting for two months, examination showing an erosion of the cervix which was bleeding. The blood and urine examinations were again negative. The following day, dilatation and curettage were carried out and a biopsy was made which showed a squamous carcinoma with cornifica-

tion (Memorial Group 2). Radium was applied by standard technic; a tube containing 101.2 mgm. in a silver container, a brass screen, the whole covered with rubber, was placed in the cervix and retained for twenty-four hours for a total application of 2,428.8 mgm. hours.

The patient was again admitted October 5, 1928, with symptoms of intestinal obstruction. Laparotomy revealed the intestines adherent to the uterus, causing an obstruction which was relieved by separating the adhesions. There were no urinary symptoms; urine and blood examinations were negative on this occasion also.

On February 8, 1930, the patient was again admitted, with a history of pain in the right side of the abdomen of four months' duration, which was temporarily relieved by the occasional passage of large quantities of urine. For one month she had been incontinent when relaxed. X-rays showed no metastasis. Urological examination showed a large right kidney, no bladder ulceration, a normal left kidney, a stricture of the right ureter 4 cm. from the orifice, and a ureterovaginal fistula distal to this point. Excretory urograms revealed a functionless right kidney which was removed, the patient making a satisfactory recovery. The kidney showed an advanced pyonephrosis with no carcinomatous invasion.

Fifteen months later this patient again entered the hospital with an intestinal obstruction, and died following an intestinal resection for carcinoma of the bowel. Autopsy showed the lungs and remaining kidney unaffected, fatty degeneration of the liver, and diffuse carcinomatous invasion of the body of the uterus, and of the intestines.

Case 2.—Mrs. M. F., aged forty-five, was admitted to the hospital April 21, 1930, with a history of eleven pregnancies, nine normal deliveries, but incidental lacerations of the cervix and pelvic floor, and two curettages. Menstruation had been increasing in amount. She had no urinary symptoms; urine and blood examinations were negative. Examination showed lacerations of the cervix and pelvic floor. Dilatation and curettage, biopsy, and repair of the lacerations were followed by an insertion of radium, 101.2 mgm. and three needles for a total of 1,787.5 mgm. hours. Pathologic report was hyperplasia of the endometrium.

The patient was readmitted October 16, 1930, with a history of left-sided abdominal pain. The left kidney was large; urological examination showed no bladder growth nor ulceration; the right kidney was normal; the left ureter obstructed at 5 cm. from the orifice. Excretory urograms showed a functionless left kidney which was removed, the patient making a satisfactory recovery. The pathologic report was pyonephrosis.

Case 3.—Mrs. M. L., aged forty-three, was admitted to the hospital January 30, 1931, with a history of lacerations at childbirth sixteen years previously, a feeling of weight in the lower abdomen,

irregular vaginal bleeding for four weeks; no urinary symptoms. A mass was palpable in the lower abdomen, which, on removal, was reported to be a pseudomucinous, papillary cystadenoma of the right ovary, probably with beginning malignant degeneration. Blood, urine and Wassermann examinations were negative. She was readmitted three months later, having at this time a profuse vaginal discharge. Urine and blood examinations were again negative. Biopsy of the cervix showed adenocarcinoma of the corpus uteri. The cervix was dilated, tandem tubes of radium were inserted with the regular protection for a total of 2,428.88 mgm. hours. Four weeks later, April 30, 1931, dilatation and curettage were carried out, and on May 18, 1931, the same dosage of radium was given high up in the uterine cavity (total irradiation 4,857.68 mgm. hours).

On July 1, 1931, the patient was readmitted and a complete hysterectomy and left salpingectomy were done. The uterus was found to be free of carcinoma, but sections of the ovary showed cystadenocarcinoma. On July 6, 1931, neither kidney was palpable; the bladder mucous membrane was congested throughout, with bullous edema of the base obscuring the right ureteral orifice; the left ureter and kidney were normal. Following an intravenous injection of indigocarmine, the right ureteral orifice was visualized, and, on passing a catheter, an obstruction was encountered at 4 cm. from the bladder, with a ureterovaginal fistula distal to this point. A course of deep x-ray therapy was given over a period of four weeks.

The patient was readmitted and given a transfusion for the anemia then present. On October 13, 1931, the right kidney was removed and showed advanced pyonephrosis. The patient then remained in good health until eighteen months ago when ascites reappeared, and she has since been under x-ray therapy. She has been free of urinary symptoms.

Case 4.—Mrs. I. C., aged forty-seven, was admitted to the hospital April 9, 1931. One brother had died of tuberculosis. Artificial menopause had been induced twelve years previously by a hysterectomy, but irregular vaginal bleeding had been present for ten months. Blood, urine, and Wassermann examinations were negative. Biopsy of the cervix showed squamous carcinoma, Group 2 and Group 3. One tube of radium (101.2 mgm.) was placed in the cervix for twenty-four hours, and three needles (12 mgm. each) were inserted in the anterior lip of the cervix and laterally for twenty hours, making a total irradiation of 3,146.88 mgm. hours.

On June 17, 1931, the patient was readmitted with a vaginal hemorrhage. A cystic mass was palpable in the left pelvis. Deep x-ray therapy was given, and two transfusions for the anemia. The urine at this time showed blood and pus cells with a negative culture. The patient had marked frequency with no pain or dysuria, later followed by incontinence. Pain was present in the left costovertebral angle;

the left kidney was palpable and tender. Cystoscopic examination showed a normal right kidney, an obstruction of the left ureter at 4 cm. from the bladder, and a ureterovaginal fistula distal to this point. Following a transfusion, a left nephrectomy was carried out, the pathologic report showing renal tuberculosis. There was no evidence of radium reaction in the bladder, and recent follow-up examinations have shown the cervix, vagina, and pelvis to be healthy, with no urinary symptoms or bladder lesions present.

Case 5.—Mrs. K. B., aged thirty-nine, was admitted to the hospital April 30, 1923, with a history of metrorrhagia of three months' duration. She had had a laparotomy sixteen years previously, fibroids and a tube and ovary being removed. Examination revealed a mass in the cervix extending into the right vaginal wall. Biopsy showed squamous carcinoma. Following a dilatation and curettage, a tube of radium (101.2 mgm.) was placed in the cervix for twenty-four hours, and two needles (25.16 mgm.) were inserted in the cervix and adjacent vaginal wall for the same length of time. Urine, blood, and Wassermann examinations were negative.

On November 11, 1923, a small nodule being present in the anterior lip of the cervix and a second in the posterior fornix, the patient was readmitted and four radium needles (50.40 mgm.) were inserted for twenty-four hours, the total irradiation to that time being 4,242.24 mgm. hours. Eight years later the patient was readmitted for treatment for a severe sciatica, an injection of normal saline with novocain being made into the caudal canal. Two month later (March 9, 1932), she developed a thrombophlebitis of the right leg and thigh. X-rays showed no metastasis; blood and urine examinations were negative.

Three months later (June 6, 1932), the patient was again admitted with a large tender right kidney. Cystoscopic examination showed no bladder lesions, a normal left kidney, an incomplete obstruction of the right ureter and a right pyonephrosis. A nephrectomy was done, the patient making a satisfactory recovery.

Case 6.—Mrs. J. D., aged thirty-eight, was admitted to the hospital July 31, 1930, with a history of vaginal bleeding for seven months. There had been fourteen pregnancies from which severe lacerations had resulted; partial incontinence had been relieved by operative repair. Examination showed laceration and erosion of the cervix. At operation, a curettage and amputation of the cervix were carried out, sections of the cervix revealing carcinoma, Groups 2 and 3. A tube (101.2 mgm.) of radium and four needles (48 mgm.) were inserted, the latter pointing toward the broad ligaments, all being retained for twenty-four hours, for a total irradiation of 3,580.8 mgm. hours. A course of deep x-ray therapy was given. Blood and Wassermann tests were negative; the urine showed a few pus cells and colon bacilli.

On April 17, 1931, the patient was readmitted with a small nodule in the cervix. Three radium needles (30 mgm.) were inserted for eight hours, 288 mgm. hours being given. Cystoscopic examination at this time showed congestion of the entire bladder, an incomplete obstruction of the right ureter at 4 cm., a slight diminution of function of this kidney, with a few pus cells and colon bacilli, the left kidney being negative.

The patient was kept under observation, the right kidney gradually becoming functionless. Although the patient was in extremely poor general condition, a series of four transfusions was given and a right nephrectomy was done (June 28, 1932). It was necessary to remove a large area of the peritoneum, and the liver showed metastasis. The patient succumbed three days later.

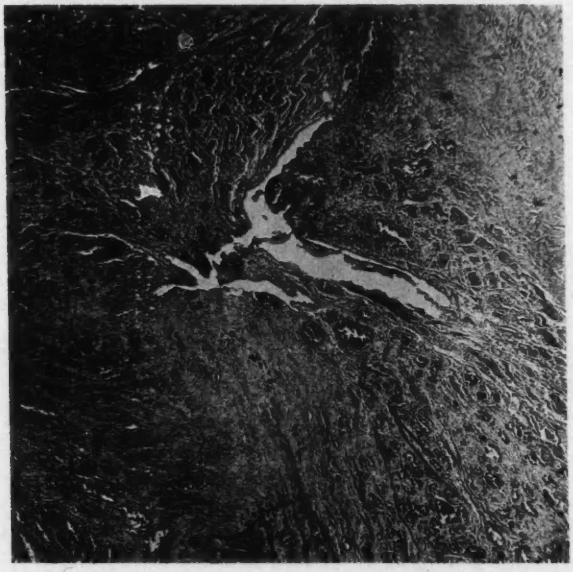


Fig. 1. Case 7. Section of occluded ureter showing carcinoma in the ureteral wall, also fibrosis.

Autopsy showed no metastasis in the remaining kidney, but diffuse squamous carcinoma throughout the uterine muscle, extending to the pelvic fascia, retroperitoneal glands, retroperitoneal connective tissue, and peri-bronchial lymph nodes, with fatty degeneration of the viscera.

Case 7.—Mrs. A. H., aged seventy-eight, was admitted to the hos-

pital November 22, 1933, with vaginal bleeding of ten days' duration, the history being otherwise unimportant. Examination showed the cervix destroyed by carcinoma, Group 3. The blood showed a moderate anemia; the urine examination was negative. At biopsy, large chunks of carcinomatous tissue which extended to the vaginal surface were removed. Radium tubes (101.12 mgm.) were inserted for twenty-four hours for a dosage of 2,426.89 mgm. hours. The patient was discharged December 2, 1933, was readmitted December 26, 1933. Her history during the three weeks subsequent to discharge showed pain in the lower abdomen during urination, frequency, vomiting for a week, and anuria for forty-eight hours. Examination re-

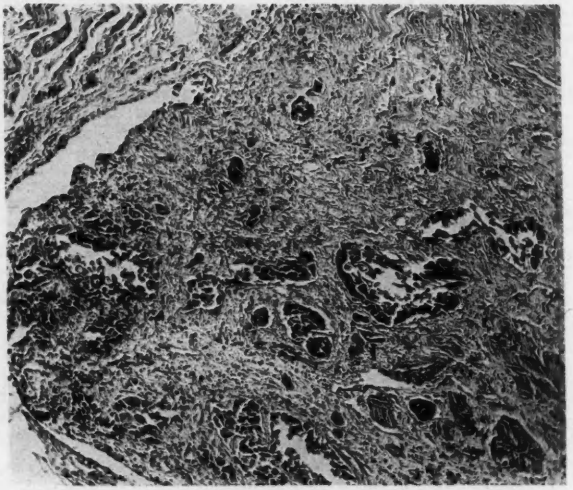


Fig. 2. Same as Figure 1 (high power).

vealed tenderness over the lower abdomen, also in the region of the left kidney and along the course of the left ureter. There was a profuse purulent discharge from the utero-cervix. The blood showed a pronounced anemia and nitrogen retention; Wassermann test was negative. The first cystoscopic examination was made seventy-two hours after the onset of the anuria. At this time the kidneys were not palpable; the bladder showed congestion throughout, no evidence of growth; the ureteral orifices were elevated; 3 cm. from the bladder, catheters encountered an obstruction in each ureter which was passed. The urine from each kidney contained no pus cells and was sterile. The catheters were retained for three days, then removed. Four days

later catheters were reinserted with much difficulty owing to a more pronounced obstruction of the ureters. X-rays were negative for calculus or metastasis. The patient died eight days later.

Autopsy showed, in both kidneys (particularly the left), a parenchymatous degeneration, mainly in the tubular apparatus, with focal and diffuse inflammatory infiltration leading to the formation of abscesses and phlegmonous dissemination. Both suprarenal glands showed parenchymatous degeneration. The uterus and firm portions of the broad ligaments involving the ovaries and tubes were extensively permeated by squamous carcinoma with frequent necrosis. The upper ureters were distended, while below, carcinoma was shown in the ureteral wall, on microscopic section, and the mucosa was, in places,

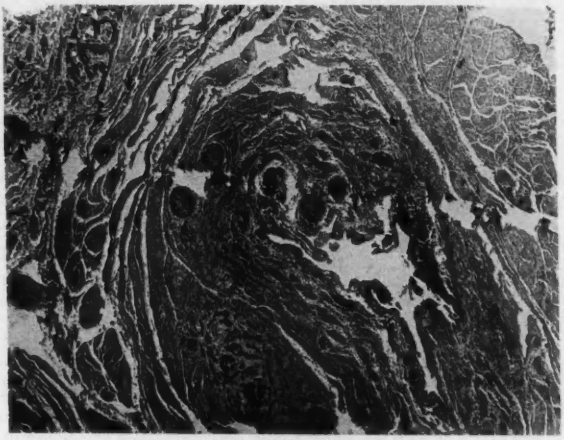


Fig. 3. Case 8. Section of occluded ureter showing carcinoma in the ureteral wall, also fibrosis.

replaced by carcinomatous tissue, the periphery of this portion of the ureters being sheathed in carcinoma and connective tissue, causing occlusion from pressure. The bladder mucous membrane was congested, but showed no invasion of the growth. There was no carcinomatous metastasis in any parenchymatous organ.

Case 8.—Mrs. M. S., aged forty-four, was admitted to the hospital February 24, 1930, with a history of being treated elsewhere for carcinoma of the cervix two years previously. Radium had been applied to the vaginal surface, also over the pubic region and deep x-ray therapy given. One year later, she developed a vesicovaginal fistula. A suprapubic opening was made preparatory to a repair of the vesico-

vaginal fistula; on opening the bladder, however, a large calculus was found and removed, no attempt being made to complete the operation at this time. On February 3, 1931, an attempt to close the fistula resulted in failure, but on November 25, 1931, it was successfully closed. On October 3, 1933, the patient was seen in the Urological Clinic suffering from pain in the left kidney region. Cystoscopic examination showed the bladder capacity normal, congestion of the entire bladder, no ulceration or growth; the right ureter and kidney were normal, while the left ureter was obstructed at 5 centimeters. One week later, a catheter could not be advanced beyond 3 centimeters.

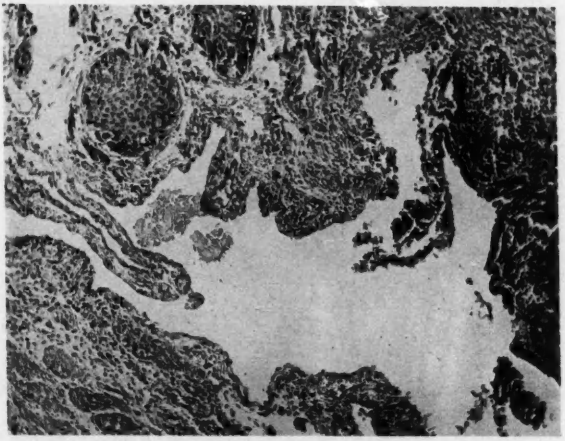


Fig. 4. Same as Figure 3 (high power).

On March 30, 1934, the patient was admitted to the hospital suffering from hemorrhages from the bowel, and died April 11, 1934. Autopsy showed extensive carcinoma of the intestines, also of the uterus, extending into the broad ligaments and surrounding the left ureter, the lumen of which was compressed and nearly obliterated by the growth. The ureter above this point was dilated and the left kidney was completely destroyed.

All these patients, with the exception of the last one, were admitted to the hospital compaining of vaginal bleeding; all but one showed a squamous carcinoma of the cervix on biopsy; all except the last one were treated at the Woman's Hospital with radium, one or more tubes being inserted into the cervical canal for a minimum dosage of 1,787.5 mgm. hours, and a maximum dosage

of 4,857.68 mgm. hours. In three cases needles were also inserted into the cervix, and five patient had received deep x-ray therapy. In four cases the carcinoma had extended into the vaginal wall. None of these patients showed evidence of metastasis when first treated. None had urinary symptoms at the time of the first irradiation; and in all but one the urinalyses were negative. All had a negative Wassermann examination. The ureteral obstruction was unilateral in seven cases and bilateral in one; the average distance of the obstruction from the ureteral orifice was 4 cm., and in three cases there was a ureterovaginal fistula distal to this point.

In the first six cases a functionless kidney due to pyonephrosis and secondary to a ureteral occlusion was removed, the time elaps-

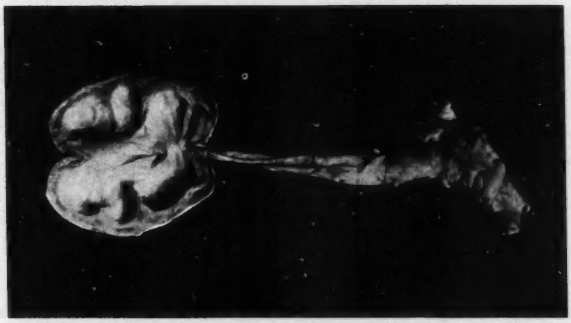


Fig. 5. Case 8. Occlusion of lower ureter with dilatation above and complete destruction of kidney.

ing between the irradiation and the nephrectomy being as follows: (1) twenty-two months, (2) seven months, (3) five months, (4) seven months, (5) twenty-two months, (6) nine years. Of the two patients not operated on, the bilateral obstruction in Case 7 occurred one month after the irradiation, and in Case 8, five years. None of the kidneys removed showed metastasis; one was tuberculous when removed, but negative at the time of irradiation.

Dean describes three radiation reactions in terms of surface reaction: the first, an irritation occurring within twenty-four hours; the second, an erythema appearing at the end of a month and due to a temporary, localized, vasomotor paralysis which may progress to tissue destruction; the third, formerly called a delayed radium

burn, like the second, is a specific radiation change, and is due to an obliterative endarteritis. The cases of bladder injury that he reported were of the third type and appeared in a minimum of ten months after irradiation.

In Dean's cases, the bladder lesions were in an organ which had not apparently become invaded with carcinoma, and were not due to a breaking down of carcinoma tissue; while, in these cases of ureteral occlusion (in two cases that came to autopsy) carcinoma was found to have extended to or metastasized in the occluded ureter. It is quite possible that in the other cases the growth had extended in a similar manner and that the early breaking down of the tumor tissue after irradiation, with the rapid cicatrization which had resulted, had accounted for the early ureteral occlusion, also the establishment of a ureterovaginal fistula in three cases. Smaller doses of radiation were given in these cases than were given in Dean's cases, which probably accounts for the absence of bladder lesions, except in Case 8, the patient having been radiated elsewhere.

In the seventh case, in which there was an obstruction of both ureters one month after irradiation, the microscopic sections of the ureters and adjacent tissue showed carcinoma and cicatricial tissue in the ureters and surrounding tissue. The same microscopic picture was present in Case 8.

The results obtained by irradiation in the treatment of cervical carcinoma have been such as to warrant its general employment in such cases. The possibility, however, of ureteral occlusion, either unilateral or bilateral, secondary to its use, resulting in the slow destruction of a kidney, possibly necessitating nephrectomy, must be considered.

In the follow-up examinations of these patients after irradiation, the urinary tract should receive careful attention. Urinary examinations should be made regularly and be supplemented by excretory urograms and cystoscopic investigations, when symptoms or physical signs are present which suggest the possibility of ureteral occlusion.

REFERENCE

1. Dean, Archie L., Jr.: Injury of the urinary bladder following irradiation of the uterus. Amer. Jour. Obst. and Gynec., 25:667, (May) 1933.

CALCIFIED TUBERCULOUS MESENTERIC LYMPH NODES

ARTHUR H. PAINE, M.D.

Rochester, New York

The precision of upper urinary tract diagnosis has done much to assist the internist and surgeon with atypical and unusual diagnostic problems within the abdomen. Recognizing this ally, the careful, conscientious surgeon requests urologic consultation in a constantly increasing number of perplexing abdominal cases.

The frequency with which a report of "negative findings in the urinary tract" has to be made is impressive. While this information is undoubtedly of value in ruling out these organs as a source of pathology, both the referring physician and the patient often look askance and seem to feel they have received little for the trouble and expense involved.

It is not advisable for the urologist to make and sponsor a diagnosis not involving his special field, but if he is familiar with the various lesions and conditions simulating urinary tract symptomatology, suggestions directing further study and investigation may prove valuable.

A condition, while infrequently seen by the urologist, which deserves our consideration is tuberculous mesenteric lymphadenitis. Under the term tabes mesenterica the condition has been recognized since the middle of the eighteenth century.[6]

An excellent review of the literature and discussion of the modern concepts and knowledge of the disease with eight case reports has been published by Golden and Reeves.[3]

The disease is one of childhood and early adult life. The chief accredited source of infection is milk from tuberculous cows. When tubercle bacilli are recovered from mesenteric lymph nodes, the bovine type occurs in 59 per cent of the cases.[4] Studies have seemed to establish the fact that, without producing lesions in the intestine, tubercle bacilli pass through the intestinal wall to the mesenteric lymph nodes.[2, 5]

The location of the infected nodes is most common in the lower portion of the mesentery of the ileum, mesial to the cecum and

ascending colon. When calcified, roentgenograms show them below the third lumbar and above the second sacral segment. While occurring on both sides of the spine the predominance is on the right. Often they lie near or in the line of the course of the ureter.

Stereoscopic and lateral roentgenograms with leaded catheters, will show the calcified glands to lie intraperitoneally well anterior to the plane of the ureter and thus differentiate them from ureteral calculi or retroperitoneal glands.

Pathologically, any stage of tuberculosis may be found in affected nodes. The incidence of calcification increases with the age of the patient up to 58 per cent. Clinically, the prominent symptom is pain, usually in the right lower quadrant of the abdomen.

In character, the pain may be a dull ache or a sharp colic frequently radiating to the back and groin or thigh. When colicky the occurrence is in intermittent attacks and may be accompanied by nausea and vomiting. Fatigue, physical activity and menstruation, as in the case herein reported, tend to precipitate the attacks. It is not surprising that this group of symptoms should suggest ureteral colic.

Abdominal palpation finds tender areas in the right lower quadrant, some rigidity and occasionally a localized mass. The patient in the case reported herewith had flexion of the thigh.

It must not be inferred that mesenteric lymphadenitis always gives rise to symptoms or represents more than silent calcified healed tuberculous lesions.

Diagnosis is made by exclusion of all intra-abdominal pathology which the symptoms may simulate, and by the roentgenogram when calcification is present. The leaded ureteral catheter is of great value to localize the shadows. The leukocyte count is not elevated.

When a diagnosis is possible the general hygienic treatment of tuberculosis is instituted. Only when the symptoms are severe enough to incapacitate the patient or cause chronic invalidism is surgical excision justified. A danger of disseminating generalized tuberculosis by surgery exists and such cases are reported.[1]

The nodes are often intimately attached to a large branch of the mesenteric artery and complete removal is restricted by the danger of injury to the blood supply to a loop of intestine.

Two slides demonstrating calcified mesenteric lymph nodes are presented. The location and appearance of the shadows are nearly identical (Figs. 1 and 2).

CASE REPORTS

Case 1.—The case showing the duplication of ureters and kidney pelves (Fig. 1) is that of a woman thirty-nine years old, who had a

Fig. 1.

Fig. 2.

recurrent cystitis and urethritis, with uninfected urine from both the pelves. A careful history failed to disclose any symptoms, past or present, referable to the calcified nodes.

Case 2.—A white woman, thin, ill nourished and sallow, aged thirty, II para, housewife (Fig. 2).

The father has arrested tuberculosis. The mother is a chronic invalid, with a history of seven major operations. There is one brother, who has peptic ulcer.

The patient complained of (1) aching pain in right loin, right lower quadrant and groin, aggravated by physical exertion, fatigue and menses; (2) inability to extend right thigh when lying supine; (3) "pulling sensation" in the right groin during urination, and slight day frequency, and (4) chronic exhaustion.

In childhood she had typhoid fever and pains in the right loin, right lower quadrant and right thigh, for which at the age of ten appendectomy was performed without relief. For the same symptoms she has had curettage of the uterus, cauterization of the cervix, and two years ago a left salpingo-oöphorectomy and Oldhausen suspension of the uterus, all without relief.

The patient has had the above described pains since before the age of ten. They are greatly aggravated during pregnancies and relieved after delivery. For the past two years she has had a chronic state of exhaustion and pain.

Physical examination revealed no abnormalities above the diaphragm. There was a slight secondary anemia and normal blood chemistry. The abdomen was thin walled and flat. There was marked muscle spasm in the right side from just above the umbilicus to the groin. The right thigh was flexed as extension aggravated the pain. Points of tenderness were found in the right costovertebral angle and right lower quadrant, most marked just below and lateral to the umbilicus. Bimanual pelvic examination gave negative findings. The left kidney was not palpable. The lower pole of the right descended below the costal margin on inspiration.

A complete study of the urinary tract revealed normal urine, normal bladder, equal good differential kidney function and normal pyeloureterograms.

The roentgenogram showed a rather disseminated group of calcified glands opposite the interspace between the fourth and fifth lumbar vertebræ and lateral to the course of the ureter. They seemed to be on the edge of the psoas muscle and were thought to be retroperitoneal in location. Study of the films stereoscopically, and at a later date a lateral film with a leaded catheter in the ureter, demonstrated the shadows to lie well anterior to the course of the ureter within the peritoneal cavity.

This case is an example of another patient who had seen many physicians and submitted to much surgery in quest of relief from one persistent group of symptoms.

The urologic examination gave only negative findings.

The group of calcified glands were interesting and stimulated a perusal of the literature and a study of case reports.

The general surgeon who referred this patient was given the information and references to the literature, which resulted in the removal of the calcified tuberculous lymph nodes.

Upon opening the peritoneal cavity the nodes were readily located in the base of the mesentery of the small intestine just above and internal to the ileocecal junction. The group of glands and accompanying fibrous tissue surrounded a large, tortuous, pulsating branch of the mesenteric artery. Danger of injury to this vessel made the removal of the nodes difficult.

Relief of pain occurred early in convalescence which was complicated by an attack of pleurisy, a condition which may be significant. The flexion of the thigh disappeared, and a recent communication from the patient's surgeon reports relief of symptoms and improvement in her general health.

REFERENCES

1. Cornet, Edred M.: The surgical treatment of tuberculous glands of the mesentery. Lancet, II:1825, 1905; Lancet, II:1913, 1908.
2. Dobroklonski, V.: De la pénétration des bacilles tuberculeux dans l'organisme à travers la muqueuse intestinale et du developpement de la tuberculose expérimentale. Arch. des méd. expér. et d'anat. path., 2:253-271, 1890.
3. Golden, Ross, and Reeves, Robert J.: The significance of calcified abdominal lymph nodes. Am. Jour. Roent. and Rad. Therapy, 22:305-316, 1929.
4. Hart, C., and Rabinowitsch, Lydia: Beitrag zu der Frage nach der Häufigkeit der Infection des Menschen mit dem Typus Bovinus des Tuberkelbazillus in den Kriegsjahren. Ztschr. f. Tuberk., 27:334, 1917.
5. Martin, Sidney: Allbutt's System of Medicine. 2:21, 1905.
6. Randall, A.: Tabes mesenterica. A case report. Jour. Urol., 15:493-497, 1926.

DISCUSSION

DR. F. H. HAGNER (Washington, D. C.): I would like to report a case along the line reported by Dr. Bugbee. Some two years ago, I was asked to see an old lady in the hospital who had not passed any urine for twelve days. She had a history of having had carcinoma of the cervix and was treated at Dr. Kelly's sanatorium. I was able to catheterize both ureters, but there was no flow of urine obtained and we allowed the catheters to stay in for forty-eight hours. During that time she secreted less than 2 ounces of urine.

Two days later the catheters were re-inserted and during the following forty-eight hours she secreted less than an ounce of urine. This woman's non-protein nitrogen was high and her creatinin was high but she had none of the classical symptoms of uremia. She was given the usual treatment, salt solution, glucose and so forth, with no result. She died on the twenty-eighth day, having secreted less than 4 ounces of urine in twenty-eight days. She died from exhaustion, as I said, without any symptoms of uremia. At autopsy the bony pelvis was filled with fibrous tissue. It looked almost as if wax had been poured into the pelvis; you could see the undilated ureters coming in on each side. We injected fluid into the ureters and with difficulty the fluid passed into the bladder. Neither ureter was dilated. The kidneys were almost infantile in type and there was a moderate amount of sclerosis but no hydronephrosis.

This woman's blood pressure had been moderately high, but not exceptionally so. The interesting feature in this case to me was the length of time she lived without passing any urine. It was almost exactly as though both ureters had been simultaneously cut off, as there was no dilatation of the pelvis and no dilatation of the ureter.

DR. GEORGE R. LIVERMORE (Memphis, Tenn.): I would like to cite a case following Dr. Bugbee's presentation, which shows the value of nephrostomy in this type of case. This patient, a woman thirty-nine years of age, had had carcinoma of the cervix and been treated by radium and deep x-ray. The gynecologist had seen her

four weeks before and had felt that the carcinoma had been controlled. Obstruction of the ureter was due to induration following the implantation of radium. She had had a nephrectomy four years before, and with the ureter from her one remaining kidney so obstructed, she had excreted only 4 ounces of urine in the preceeding forty-eight hours. She was unconscious from uremia, with a blood non-protein nitrogen of 165 and a creatinin of 4.8. Under novocaine and ethylene a nephrostomy was done. The pelvis and ureter were dilated and 45 c.c. of clear urine obtained when the nephrostomy was done. Urine was dripping from the tube before she left the operating room and she excreted 4000 c.c. of urine in the next twelve hours. She has continued to improve and when I left home ten days after her nephrostomy, she was free of all uremic symptoms and excreting 1200 to 1500 c.c. in twenty-four hours.

DR. ALEXANDER RANDALL (Philadelphia, Pa.): I see a very close analogy between the cases reported by Dr. Bugbee and the ones I reported the other day. I was dealing with carcinoma of the bladder and he was talking on the subject of carcinoma of the cervix. I would like to raise the question for Dr. Bugbee to answer whether or not he feels radium had anything to do with the picture at all. Fortunately he has had the opportunity, which I have not had, of having the renal pathology in his hands. I think the most interesting features to us may be summed in two questions: first, what can be done or what should be done by us surgically to relieve exactly what Dr. Livermore has just reported, an inevitable uremic death, whether or not these kidneys can be saved, and if so, how? Second, how can we explain the physiologic fact that goes on here? I don't know that we see kidneys like this in any other place.

Dr. Hinman talks about his primary atrophy. That is all right if you are going to have a sudden occlusion of a ureter, but I can't picture this condition as anything else but a slow occlusion. I think it is a most interesting thing. I don't know but that we are bordering on some new behavior in regard to kidney function, where, as in Dr. Bugbee's cases that have been reported, and mine, you witness a slow renal death, a symptomless renal death.

DR. NATHANIEL P. RATHBUN (Brooklyn, N. Y.): I should

like to add very briefly one case to Dr. Bugbee's group which I think presents a little variation in the symptomatology and course from some of the other cases. There was a woman I saw several years ago who had been treated two years before, apparently fairly successfully, for carcinoma of the cervix by radium. I don't know the dosage or just how it was applied. Apparently at least that was controlled. When I saw her, she had had total anuria for eight days. We brought her to the hospital and made a cystoscopic examination; I found nothing that, to my mind, suggested either carcinoma or radium damage of the bladder. The ureters appeared reasonably normal, but no form of catheter or bougie could be passed. It could be engaged, but not passed. She, of course, was profoundly uremic with marked evidences of nitrogen retention.

We then turned her over on her side and with a local anesthetic did a nephrostomy arbitrarily on the right side, I think. We found a huge hydronephrosis with the kidney cortex very materially thinned out, and put in a nephrostomy tube. The following two days she secreted huge quantities of urine from this nephrostomized kidney, but her general condition did not improve at all.

Under local anesthesia, we did nephrostomy on the other side and found a huge extrarenal hydronephrosis and a good looking kidney. We did a nephrostomy on that side, apparently too late, for she died about forty-eight hours later.

I had a feeling that if I had been fortunate enough to select the other side first, or if we had done a bilateral nephrostomy, she would have had a better chance. We had no lead, of course. My interpretation of this case was a little bit different from most of the cases Dr. Bugbee reported. I interpreted my case as a fibrosis of the lower end of the ureter rather than carcinoma. Unfortunately, we could get no autopsy, so I am not sure what the actual conditions were.

DR. GILBERT J. THOMAS (Minneapolis, Minn.): I have had some experience with my gynecologic friends in treatment of carcinoma of the cervix. I think we should coöperate with them a little more than we do, rather than criticize them. In the first place, you may or may not know that carcinoma of the cervix is the one remaining cancerous lesion that seems to lend itself to irradiation with radium, with the hope of cure. This being the case, the urolo-

gist must assist the gynecologist when he uses radium for this purpose whether it be a radium pack, needles, or emanations. When these are put into the cervix, the vagina is thoroughly packed and in most instances after the patient leaves the operating room she cannot urinate because the urethra is thoroughly compressed by this packing. I advise my gynecologic friends to put in a permanent urethral catheter at the same time that the packs are put into the vagina.

I also advise that the patient be given cystoscopic examination within the first three or four weeks following the use of radium. The bladder is examined for evidence of radium irritation and possible metastasis; the function of the ureters and kidneys is observed but ureteral catheterization is not done at this time. If in doubt concerning the function of the ureters, an intravenous urogram may be made. When the effect of the irradiation is at its height or when it should be going down, the cystoscope should be passed, and an intravenous urogram may be made.

I recently had a disagreeable experience during which I found a dilated ureter and an infected kidney, which I am sure was present before radium was used, but which was blamed on the effects produced by the radium. I, therefore, suggest that before radium is used in the cervix, a cystoscopy should be done, and an intravenous urogram made.

Dr. Thomas C. Stellwagen (Philadelphia, Pa.): I would like to add a case of calcified lymph nodes. A patient was brought to me who had all the symptomatology of an obstructive lesion to the ureter, and upon radiographic study a mass of calcified lymph nodes was found in close contact with the ureter. I approached them through an abdominal incision. She had insisted on avertin anesthesia. They were removed, and in so doing there was considerable trauma delivered to the vasa intestini tenui. Three days afterwards, we thought she had a paralytic ileus because we had seen a similar condition occur after avertin anesthesia. I subsequently opened the abdomen and found she had an apoplexy of the mesentery. Resection of the small intestine was done, followed by an end-to-end anastomosis and the patient recovered. I have had two of these cases and in both instances found that the removal of the glands was quite a problem to the circulation of the bowel.

DR. ROGER C. GRAVES (Boston, Mass.): Dr. Bugbee's paper is a very timely one and the length of this discussion is evidence enough of the fact that he presents an important subject and one that we are going to have to deal with more and more as time goes on. I am confronted with the sort of problem that he describes, quite often, in our state cancer hospital in Massachusetts. I have at the present time under my care in another hospital a woman upon whom I had to perform an emergency bilateral nephrostomy five days after she had a hysterectomy, to relieve the symptoms of complete ureteral obstruction. In this case there later was found carcinoma in the cervix which had not been removed, and the surgeon had used radium and x-ray before his operation in an attempt to arrest uterine bleeding from fibroids. The patient was saved from the immediate dangers of uremia by the nephrostomies, but of course still has malignant disease in the pelvis.

Whether the occlusion of the lower end of the ureter occurs from the spread of cancer, or from the scar following radiation, or from the effect of radium itself is beside the point, as far as the effect upon the ureter and the ultimate fate of the kidney are concerned. Perhaps it is not beside the point with reference to our plan and purpose of therapy. If the patient has hopeless malignant disease of the cervix, one will operate only to relieve pain, or the distressing symptoms of infection or uremia. On the other hand, if the pelvic condition is more favorable and there is still hope of cure, one may, of course, attempt more extensive surgery in the hope of restoring to the urinary system conditions as nearly normal as possible.

The emergency operation of nephrostomy to relieve impending uremia in these cases cannot be overestimated in value. I wish merely to call attention to the fact that I find that in these very sick indivduals one can carry out the whole operation very satisfactorily with novocain alone and without any general anesthesia by blocking the tenth, eleventh and twelfth dorsal nerves and then infiltrating the line of the incision; one can complete the entire nephrostomy with nothing more than local anesthesia.

DR. HENRY G. BUGBEE (New York City): I would hardly agree with Dr. Randall that the ureteral obstruction in these cases is due entirely to growth in the wall of the ureter. In the last case

of the eight reported, in which we had an autopsy, the irradiation had been given five years previously, and there was not a large amount of carcinomatous tissue present, while there was a considerable amount of cicatricial tissue as revealed in the microscopic sections. I believe that if the obstruction had been entirely due to carcinoma, the growth would have spread more rapidly, and the occlusion would have occurred earlier than it did in most of these cases. None of these patients had urinary symptoms until after irradiation; all had had careful urinalysis when they entered the hospital and a very complete physical examination. No pus was present in the urine before irradiation, except in one case, and that was the case which later showed tuberculosis.

I believe, therefore, that the irradiation was a definite etiologic factor in causing the occlusion, and that the carcinoma which was demonstrated was also a factor. Just how much of the obstruction was due to growth and how much to cicatrix one cannot say. I believe, however, that it is more than a coincidence that the urologic complication came after the application of the radium. Furthermore, I should not have expected these patients to go on as well as they did after nephrectomy, had an extensive, active carcinoma been left in the lower ureter. In the follow-up, they have done very well as far as the local condition is concerned.

EXTERNAL PERINEAL URETHROTOMY WITH INVAGINATION AND RESECTION OF AN IMPERMEABLE STRICTURE OF THE PENILE URETHRA

JOHN R. CAULK, M.D., F.A.C.S.

St. Louis, Missouri

The necessity for operative procedures designed for the relief of stricture of the urethra has gradually diminished with time. Gonorrheal infections, which are obviously the chief cause of stricture of the urethra, have been reduced in frequency, and provision of more scientific therapy has materially reduced the incidence of serious late complications, the most important of which is stricture. The principle of gradual dilatation instituted many years ago still remains the ideal method, and the majority of urethral strictures are adequately treated in this manner. We owe a debt of gratitude to the early French school of urology which furnished us with instruments which, with but few exceptions, have been but little improved even to the present day. Civiale, Maisonneuve, LeFort, Albarran and Guyon are memorable figures in this field of surgical endeavor. Oberlander and Kollmann of the German school made outstanding contributions in the realm of pathology. Among the British investigators, Wheelhouse, Syme and Sir Henry Thompson made notable contributions, and our own Bangs, Otis, White and Keyes added their share to the knowledge of this subject. The admonition of J. William White, "Dilate if you can and cut only if you have to," has been a useful guide to follow in the treatment of stricture.

An analysis of the cases of stricture which have been observed in my private practice and in the clinics of Washington University serves to illustrate in a striking fashion the value of gradual dilatation in preference to surgical procedures. There have been 1495 cases of stricture in this series, only fifty-two of which have required urethrotomy, two internal and fifty external, or 3.4 per cent. Of this number only two internal and ten external were performed for uncomplicated stricture, five of these having been done prior to 1913. The remaining number of urethrotomies were performed for complications associated with stricture such as extrava-

sation of urine, peri-urethral abscess, fistulæ and impassable stricture. Thus the surgery of stricture is primarily the surgery of its complications. In only 0.8 per cent of all the cases was operation resorted to for simple uncomplicated stricture.

We have more or less universally accepted the advisability of surgery for undilatable and markedly resilient strictures of the penile urethra by internal urethrotomy and strictures in the deeper portions of the canal at the bulbo-membranous segment by external perineal urethrotomy.

Occasionally there are strictures in the penile urethra which resist internal urethrotomy and a variety of operative procedures have been designed to care for them. Cifuentes (Jour. d'Urolgie, 1927) proposed an operation for impassable stricture at the penoscrotal juncture, in which, through an external urethrotomy incision, a filiform is passed from behind and the stricture either dilated with followers or cut by internal urethrotomy with a Maisonneuve urethrotome threaded onto the filiform. He claims that the filiform passes readily into the urethral funnel above the stricture when threaded from behind forward, saying: "Par on passe l'urine, passe la bougie." In 1910, Gibson (Med. Record) reported a somewhat similar operation which consisted of opening the urethra behind the stricture and passing a special Coude sound, through which a filiform was passed and upon which an Otis urethrotome was later threaded.

Recently a case came under my observation which prompted me to undertake an operative procedure, which so far as I can determine has not been previously performed or reported.

A man in the early twenties came in with complete retention of urine. He had been greatly troubled with urinary difficulty for nearly two years, starting about three months after a severe gonorrheal infection, during the course of which he had voluntarily injected some strong medicine aiming at a "rapid cure" of his infection. In so doing he induced a severe reaction with pronounced swelling of the penis and considerable difficulty in urination. This acute spell gradually subsided but since then he has never urinated freely. Urinary difficulty gradually increased until his present attack of complete retention.

He entered the hospital in the evening with his bladder markedly distended. The resident urologist was unable to pass a filiform even after sedatives had been administered and hot applications applied. He was tapped suprapubically with a small trocar, through which a soft rubber catheter was introduced into the bladder. This was the third

occasion in my series of cases in which a suprapubic tapping had been performed. Drainage through the indwelling suprapubic catheter was efficient; there was never the slightest reaction. However, in spite of adequate drainage with the relief of urinary distress, repeated attempts at passage of woven filiforms through the urethral stricture proved fruitless, even fluids could not be injected through the urethra, indicating an impermeable stricture. After two weeks of suprapubic drainage,

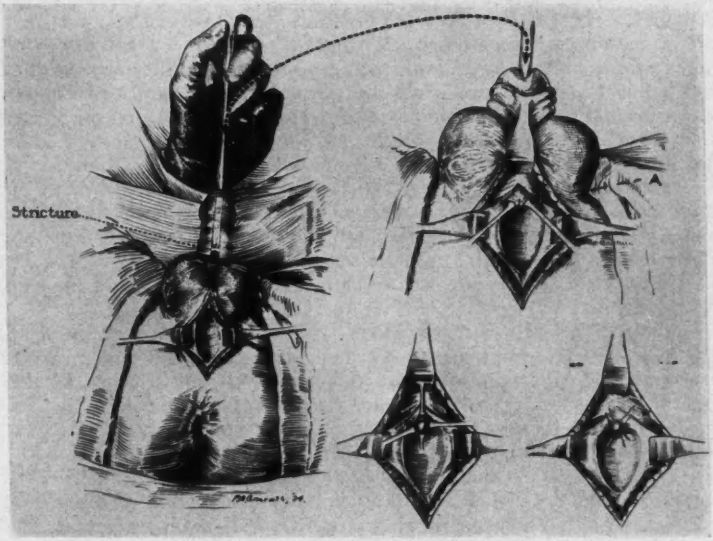


Fig. 1

during which time the stricture showed no evidence of absorption or resolution, it was still impossible to introduce a filiform or fluids. I inserted an endoscopic tube as far as the strictured area, which was situated just in front of the penoscrotal juncture, and observed a white solid scar in which I was unable to detect any opening. Therefore, it became imperative to attempt some procedure to resect this dense stricture.

Internal urethrotomy was obviously impossible, since no fluid could be introduced and external urethrotomy at this site was to be avoided. I therefore did an external perineal urethrotomy, opening the bulb in its anterior portion after bisecting the posterior portion of the scrotum (Fig. 1). The bulbous urethra at this point was tremendously dilated,

being at least an inch in diameter; this fortunately aided localization of the strictured area later. A sound was passed through the external meatus to the stricture at the penoscrotal juncture. It was then pushed backward until the obstructing area could be seen through the dilated urethra from above. The circular scarred area was then grasped with Allis clamps and invaginated into the bulbous urethra (Fig. 1, A), the assistant aiding this maneuver by pushing the sound gently from the front. The strictured segment was then incised vertically until the sound could be passed through it. It was almost a quarter of an inch in breadth. It was then resected circularly until the annular band was completely removed. Before excising the strictured area completely, the urethral mucous membrane was grasped with Allis forceps above and below the sound and while the strictured area was being resected the proximal and distal ends of the urethra were approximated with sutures. Before the sutures were tied, the sound was removed and a No. 24 catheter passed through the site of the stricture. Sutures were then tied and a catheter was passed into the bladder for drainage and splinting. After the redundant tissue had been removed, the urethra was closed over the indwelling catheter by interrupted sutures of chromic catgut. A small rubber tissue drain was inserted and the skin and fascia closed. The suprapubic catheter was removed and the sinus curetted.

The operation was very simple in spite of the dense scar tissue. It was quite easy to invaginate the penile urethra into the perineal incision by traction and pressure without mobilization of the urethra through external dissection. The patient made an uneventful recovery. The indwelling catheter was removed on the seventh postoperative day. The patient voided normally but developed a slight perineoscrotal fistula which persisted for a short time. At the end of two weeks the urethra accepted a No. 26 F. sound without the slightest difficulty. The fistula closed after a few dilatations of the urethra and silver nitrate applications. The patient has remained well and the urethra at the end of two months is patent and free.

This operation was easy of execution, fully visualized throughout and seems to be a very efficient, safe and acceptable method for resecting such rare impermeable strictures occurring in the penile urethra. It possesses the possible, indeed probable, application for other unresponsive strictures of the pendulous portion of the canal.

DISCUSSION

DR. THOMAS C. STELLWAGEN (Philadelphia, Pa.): We have had experiences with most of the intractable types of stricture. We wish to offer a few words in reference to the Esser graft. Esser devised a method of grafting either skin or mucous membrane that was unique. It consisted of first taking an impression of the cavity or tube to be covered. This was done with modelling compound. The graft was then cut and stretched about the model and secured in place by catgut stitches. The model with the graft in position was placed in the depression to be dermatized. This procedure assured the elimination of dead space and offered fairly even pressure to the graft. It was particularly applicable to restoration of eye sockets to facilitate the insertion of artificial eyes. We applied a similar principle to hypospadias cases after tunnelling a channel upon the venter of the penis. We used a cylinder surrounded by epidermis. In all we did eleven cases, two of which were fairly successful, both in negro twins. Subsequently, a Frenchman reported twelve successful cases. Such was not our experience. In cases of resilient intractable stricture, such as Dr. Caulk reports, we have found that urethrectomy may produce very happy results if the urethra is kept splinted by a proper catheter so as to insure proper alignment at the mesial and distal ends of the gap. I have seen two centimeters of urethra reproduce itself in such cases. Some of the end-results have been very satisfactory, where splinting was properly done and ample drainage provided for.

I wish to congratulate our president upon his brilliant result.

DR. LEON HERMAN (Philadelphia, Pa.): It is astonishing to me how few serious strictures are encountered at the present time. Of course, this is a tribute to urology in the treatment of urethritis. Once in a while we do see a very bad case, usually in the colored race. In a few cases, I think probably four or five, where there was practically obliteration of the anterior urethra, we have done a resection of the urethra and brought the proximal portion into the perineum, excluding the anterior part of the channel. In the event the stricture was so far back we couldn't mobilize enough of the proximal end to bring it to the skin surface, we have invagi-

nated a funnel of skin and anastomosed it to the edge of the ureteral segment. The chief disadvantage is the necessity thereafter of sitting down to void.

I have done a good many internal urethrotomies by the retrograde method. If a man has multiple strictures, the tightest one being the most proximal is divided by external urethrotomy, while the accompanying ones anterior to that are divided by the urethrotome introduced from behind forward.

In the case of impassable, ancient traumatic strictures which usually occur in association with fracture of the pelvis, excision of the strictured area with anastomosis of the urethral segments is, of course, the method of choice. These patients will have had a suprapubic drainage so that diversion of the urinary stream has already been provided for. In such cases, we have always employed flexible guides according to the methods suggested by Dr. Young today, the guide being held in position by silk ligatures tied to its proximal and distal ends. This guide is used for subsequent instrumental dilatation and may be kept in the urethra as long as necessary. In those cases in which the proximal segment is long enough to permit incision for drainage purposes this may be done to advantage, thus putting the suture line at rest and permitting the suprapubic opening to close more promptly.

Dr. F. H. Hagner (Washington, D. C.): I would like to make a suggestion. I haven't tried it yet, but I want to try it. Some of you may remember the case I presented of circular grafts for straightening the penis in hypospadias. I believe that that is applicable, too, either in hypospadias or where there is destruction from stricture, because I believe where there is a great destruction of urethra from stricture, and it is excised, a foreshortening of the urethra will result.

Those grafts, as you remember, are just full thickness grafts cut from the inside of the thigh. Of course, they can be made any length, and I believe that in destruction of the urethra, and possibly in hypospadias operations, we can use circular grafts for the restoration of the urethra instead of taking flaps from the penis.

Dr. Sanford: You mean your tunnel graft?

Dr. Hagner: Yes, the circular tunnel graft.

DR. ARTHUR B. CECIL (Los Angeles, Calif.): I have been very much interested in the reconstruction of congenital malformations of the genitalia in children. Many of the principles worked out in dealing with these children are applicable to the reconstruction of the urethra either in injury or stricture. If one goes over the literature of reconstruction of the urethra, either in the congenital malformations or in injuries, one is surprised to find how few of these patients have been successfully cured. For twenty-some years Nové-Josserand tried free tunnel grafts, and if you will review these cases you will find that hardly any of them was successful. The graft was either absorbed, strictured, extruded or in some instances destroyed by blood clots which formed along the tunnel in which the graft had been placed. Free tunnel grafts do not work. I have tried them and have found that the graft simply disappeared. I have re-operated in these cases and nothing of the graft was seen. I am very doubtful about the value of free grafts such as were used in France after the war for reconstruction of the urethra by using vaginal mucosa, the appendix, foreskin, et cetera. My study of this subject has led me to this belief, that only broad based pedicle grafts are likely to be successful.

DR. GEORGE R. LIVERMORE (Memphis, Tenn.): I would like to demonstrate an operation devised by a general surgeon of Memphis, Joseph E. Johnson, who is now dead. He called it his gutter operation. He removed the strictured area, leaving a small portion of the urethra, then sutured the skin of the perineum to each side of the remaining portion of the roof of the urethra. This left the floor of the urethra open, thus (illustrating). This is the mucous membrane attached here to the edge of the skin on each side. It leaves the floor of the urethra open, and when the patient voids, the urine flows out of this opening in the perineum. Then when it heals, the skin forms the lateral walls of the excised urethra. After a few months when the patient was well and all the induration had subsided, he cut the skin flaps off at each side and sutured this over a retention catheter so as to make a new wall for the urethra. The lining and floor of the urethra is the skin surface. In that way he constructed a urethra out of the skin which was attached to each side and had its blood supply established. It is just the point Arthur Cecil was making a while ago,

that you must have attachments in order that those grafts may grow. Then when they grow and are cut off, they live because they have formed new circulatory attachments. When this heals the patient has a good urethra. We have a number of such cases in the city hospital at Memphis in which this method has been used by many of the urologists on the staff, and most of them have had successful results.

THE GONADOTROPIC HORMONE IN THE URINE OF MEN WITH TUMOR OF THE TESTIS

FRANK HINMAN, M.D., F.A.C.S.
and
TRACY O. POWELL, M.D. (by invitation)
From the Hooper Foundation for Medical Research and the Division of Urology, University of California, San Francisco

The gonadotropic hormone excreted in the urine of patients suffering from neoplasms of the testicle offers many new points of interest in the study of these tumors. We shall discuss our studies on a relatively large series of cases of testicular tumor with particular reference to the following points: First, the biologic nature of the hormone; second, technical considerations of the hormonal tests; third, the value of qualitative and quantitative determinations in relation to the pre-operative diagnosis, prognosis, radiosensitivity, and histologic structure of tumors. Finally, we wish to report the facts of clinical interest encountered in the study of 105 cases of malignant tumor of the testicle, in thirty-three of which hormonal studies were carried out.

BIOLOGIC NATURE OF THE HORMONE

The testicular neoplastic hormone has been regarded as identical with the gonadotropic hormone found in the urine of pregnant women. In the early investigations of the hormone of pregnancy, it was thought to be identical with the anterior pituitary hormone. Zondek, believing that there were two different anterior pituitary hormones excreted in the urine of pregnancy, gave them the names "Prolan A" and "Prolan B." For this reason, certain writers have referred to the malignant testicular hormone as "Prolan A." Many writers, preferring not to assume the presence of two hormones in pregnancy, nevertheless adopted the term "Prolan" to designate the hormone found in the urine of pregnant women in contradistinction to the anterior pituitary hormone.

It is now definitely established, however, that the hormone of pregnancy, although similar to, is not identical with, the anterior pituitary hormone (Table I).

Similarly, from our own studies, it appears that the hormone excreted in the urine of patients with testicular neoplasms is not

TABLE I. TABLE OF DIFFERENCES

Anterior Pituitary Hormone	*Pregnancy Hormone ("Prolan")*
1. Daily transplantation of anterior lobe into immature female mice results in marked follicular growth followed by ovulation.	1. Daily injection of pregnancy urine into immature female mice causes follicular growth but with atresia of follicle and ovum, thereby preventing ovulation by transforming the follicle into a corpus luteum with retained ovum.
2. Repeated injections of anterior pituitary hormone cause an enormous increase in the weight of the ovaries in immature rats at the end of five days, often reaching 100 per cent to 500 per cent.	2. Repeated injections with pregnancy urine causes relatively slight increase in ovarian weights in immature rats at the end of five days.
3. Continued injections of anterior pituitary hormone cause very little more increase in weight of ovaries after five days regardless of period of time injections are extended over.	3. Continued injections with pregnancy urine cause the ovaries of these animals to reach enormous weights.
4. If hypophysectomized mice and rats are treated with anterior pituitary hormone, it quickly restores their hormonal deficiency.	4. If hypophysectomized mice and rats are treated with pregnancy urine, it fails to restore them.
5. In case of hypophysectomized rats and mice, the anterior pituitary hormone produces maturation of follicles followed by normal luteinization and ovulation.	5. In hypophysectomized rats and mice, injection of pregnancy urine causes only luteinization of theca cells.
6. If hypophyseal extracts (which when administered alone were devoid of any effect on the ovaries of infantile mice) are added to "prolan," maximal effects are secured.	6. If hypophyseal preparations are heated to destroy the hormone, the total effect is then no more effective than prolan alone.
7. Patients as well as animals suffering from pituitary tumors do not excrete a gonadotropic hormone in their urine.	7. Patients with chorionepithelioma and hydatidiform moles following pregnancy excrete large quantities of this hormone in their urine.

identical with the "Prolan" excreted in the urine of pregnant women. There are, however, many points of similarity.

Again in the case of male castrates, it has been established definitely that a gonadotropic hormone also is excreted in the urine. Preliminary investigations upon this hormone in other clinics indicate that it is very similar to the anterior pituitary hormone and is believed possibly to be identical. Recently Harris and Brand reported cyclical appearance once a month of gonadotropic hor-

TABLE II. HISTORICAL OUTLINE

1886	Pierre, Marie	
1901	Alfred, Frohlich	Adipose genital syndrome
1912	Harvey, Cushing	The pituitary body and its disorders
1912	Bernard, Ashner	Dwarfism and hypogenitalism after hypophysectomy
1922	Evans, Long	Experimental gigantism in normal animals —growth hormone
1924	Houssay	Insulin hypersensitiveness after hypophysectomy—contra-insular hormone
1926	Zondek, Aschheim, Smith	Experimental precocious maturity—gonadotropic hormone
1927	Zondek, Aschheim	Gonadotropic hormone in urine (A-Z Test)
1929	Smith	Anatomical changes following hypohysectomy
1929	Aron, Loeb	Thyroid changes following treatment with anterior lobe—thyrotropic hormone
1931	Reichert, et al, Engle	Difference between prolan and anterior lobe effects
1931	Fevold, et al	Anterior lobe extracts split into follicle stimulating and luteinizing hormones
1932	Riddle	Lactogenic hormone
1933	Collip, et al	Claim isolation of cortico-adrenotropic hormone (after Evans)

mone (probably pituitary) in the urine of normal men giving mature follicle stimulation in infantile animals (Reaction I).

From these facts one readily sees that in order to discuss intelligently the testicular neoplastic hormone, he must be aware of the possibility of four gonadotropic hormones excreted in the urine. Each should be referred to by its descriptive name to distinguish it from the others.

1. Anterior Pituitary Hormone
2. Prolan or A. P. L. Hormone of Pregnancy
3. Testicular Neoplastic Hormone
4. The Hormone of Castrates

The history of the discoveries leading to the demonstrations of the various anterior pituitary and anterior pituitary-like hormones in the body is unusually interesting (Table II). Time, however, does not permit us to credit properly the various investigators whose

work has added to the knowledge of any one type of these hormones. This is particularly true in the case of the gonadotropic hormones excreted in the urine. Zondek (1930) first found that the urine from a patient with a malignant tumor of the testicle may give a positive test for this hormone when carried out on immature female mice. Using the same routine he had devised for the diagnosis of pregnancy, he injected small amounts of urine five to six times in forty-eight hours and killed the animals in 100 hours with illuminating gas. In the interpretation of the tests he considered three reactions:

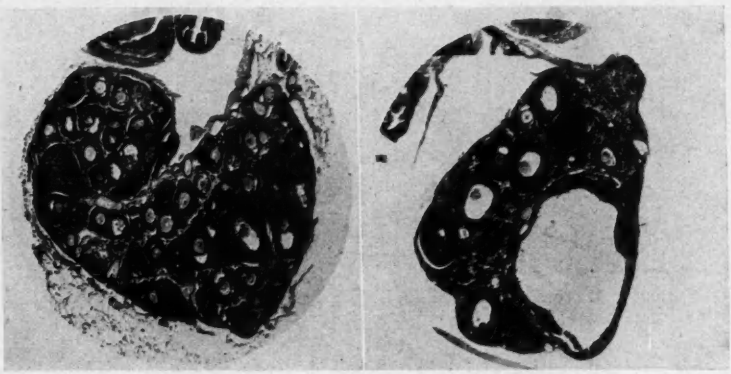


Fig. 1 (*left*). Normal ovary of infantile rat nineteen days of age.
Fig. 2 (*right*). Mature follicle reaction (R.I.). Infantile rat.

Reaction I—The immature follicles became mature. Mature Follicle Reaction (Figs. 1 and 2).

Reaction II—Hemorrhage occurred in the follicles, producing the appearance of hemorrhagic cysts or "blood points" which were easily visible. Hemorrhagic Cyst Formation.

Reaction III—Luteinization of follicles produced corpora lutea (atretic). Luteinization Reaction (Fig. 3).

Zondek at this time was aware of the presence of the follicle-ripening hormone (Reaction I) in 13 per cent of his series of extragenital carcinomas in males. (We now think this to be the result of gonadal deficiency rather than of the presence of the neoplasm.) He, therefore, concluded that Reaction I was not specific for testicular malignancy. He studied three cases of testicular tumors

at this time which failed to give positive Aschheim-Zondek tests on the patients' unaltered urine, but, by extracting the hormone by the alcohol-ether method and injecting relatively enormous quantities of urine, he was able to produce positive tests. Ferguson and his associates the following year (1931) reported several cases of

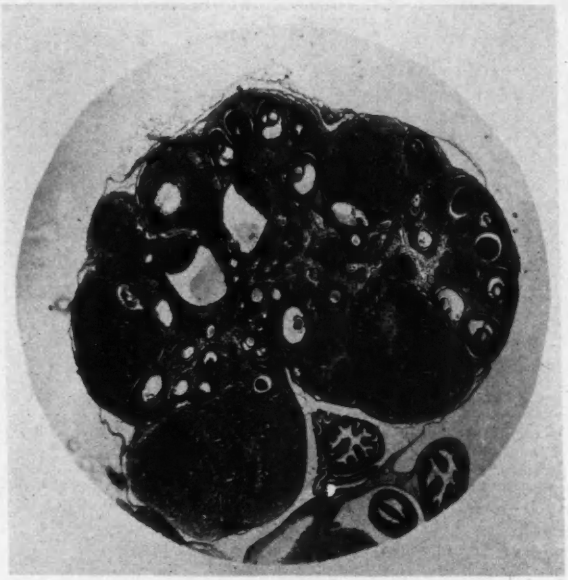


Fig. 3. Luteinization of follicles (R.III). Infantile rat.

testicular tumors with positive I, II, or III reactions. This author concluded that Reaction I (Fig. 4) was specific for these tumors. Zondek (1932) reported a series of ten additional cases of malignant tumors of the testicle, making a total of fourteen cases. In only three cases (one chorionepithelioma, one alveolar carcinoma, and one unclassified as there was no necropsy) was he able to produce positive Reaction II or III. By the concentration method, he was able to secure these reactions in only one other case. In four cases it was not possible to secure even Reaction I using concentrated urine by alcohol-ether concentration method, while in a case

of tuberculous epididymitis he was able to produce Reaction I by the concentration method.

Ferguson (1933) reported a series of 117 cases all giving definite reactions. Indeed, his table for the determination of units would lead one to think that all of these cases gave postive II or III reactions. Unfortunately this author was able to correlate the

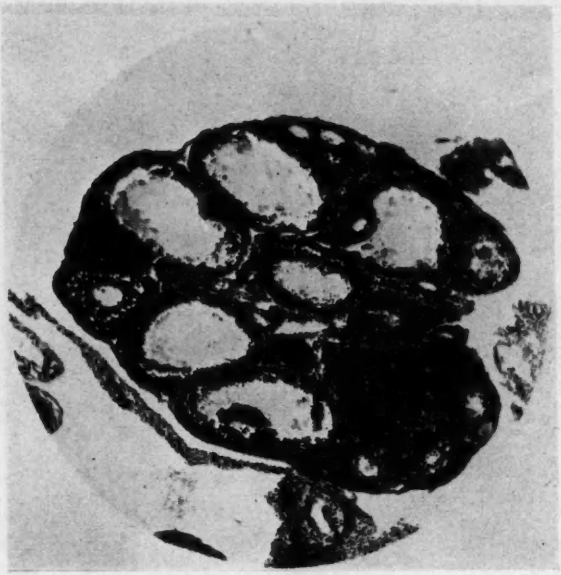


Fig. 4. Mouse ovary. Large open follicles of the castrate type.

excretion of hormone with the histologic structure of the tumor in only thirty-seven of the 117 cases.

TECHNIC OF HORMONAL TESTS AS APPLIED TO TUMORS OF THE TESTIS

We have avoided the use of the term "Aschheim-Zondek Test" because it is confusing, as it is the term applied to the test as carried out in pregnancy. In fact, all tests of pregnancy have come to be called Aschheim-Zondek tests regardless of technic or animals used.

In tumors of the testis, only infantile mice or rats should be

used as the rabbit rarely gives a postitive test. Although Zondek showed the rat to be five times more sensitive to "Prolan" than the mouse, this has not proved true in our experience with the testicular neoplastic hormone. Our experience in carrying out these tests with rats, however, has been more limited than with mice. The follicle-stimulating effect is read much more easily in the ovary of the mouse after microscopic section than in that of the rat (Figs. 5 and 6). At the present time we are using both of these

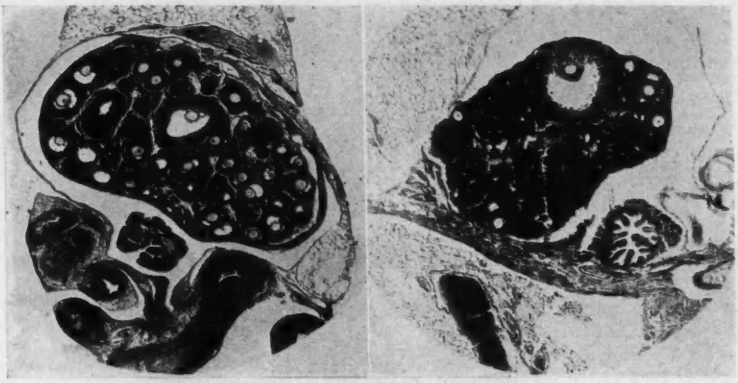


Fig. 5 (*left*). Normal infantile ovary of a rat aged twenty days, showing one moderately enlarged open follicle and illustrating the difficulty in reading microscopic sections of rat ovaries.

Fig. 6 (*right*). Mouse ovary. Early Reaction I. Only one follicle approaching maturity. More of pregnancy type of follicle stimulation.

animals as it is difficult to secure a sufficient number of either to supply our needs. We raise our own rats, thereby always knowing the exact age, which is important. These animals should be from nineteen to twenty-one days of age when used.

Even when using the mouse or rat as the test animal, the term "Negative Aschheim-Zondek Test" is meaningless in regard to tests on the urine for the testicular neoplastic hormone. One must state the quantity of urine injected or the number of units tested for, in stating that the test was negative.

At the present time, if we do not already know the hormone to be present, we routinely inject 0.2, 0.4, 0.8, and 1 c.c. of unaltered

urine, preferably the first urine voided in the morning. We believe the qualitative test is more important at first and we try to demonstrate the hormone in unaltered urine. The animals are injected subcutaneously five times in forty-eight hours and killed in 100 hours.

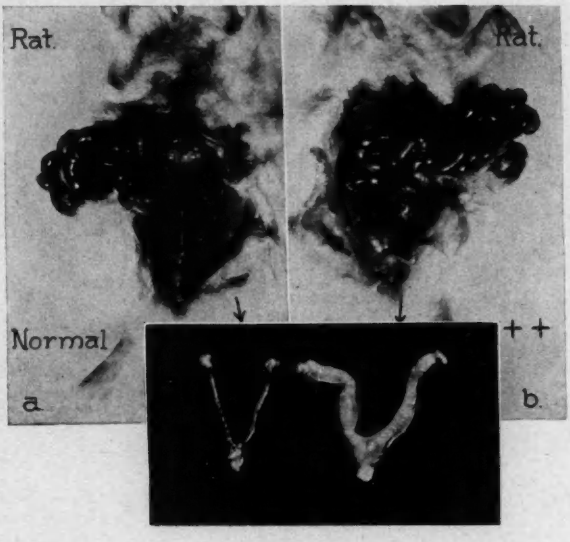


Fig. 7. Reaction read ++ grossly compared to normal. Note the large, clear uterine horns. The ovarian follicles in this case showed no stimulation microscopically.

A control animal is always sacrificed at the beginning of the test and also at the end of the test. One has the opportunity to study the normal development of the ovary in comparison with the abnormal in the microscopic sections. The gross interpretations are equally important. Our gross interpretations, unlike those in pregnancy, are concerned chiefly with the uterine horns. In the positive tests, these will be found to be enlarged often to a pronounced degree, edematous, clear and colorless. Those which we think are slightly larger and believe probably to be positive are read —1. Those with horns approaching the diameter of an ordinary match are recorded + and those with larger distention are graded ++ and

+++ (Fig. 7). The —1 is regarded negative grossly, but considerable attention is paid to these microscopically as well as to the negative tests. At present we do multiple microscopic sections on all the ovaries. It is apparent that if multiple sections are made of each ovary of the several animals used for each test, and many tests run each week, it entails considerable outlay of time and expense. For this reason we have adopted a rapid histologic technic which has proved of considerable value in our hands. The ovaries

TABLE III. TECHNIC OF EXTRACTION (MODIFIED FROM ZONDEK)

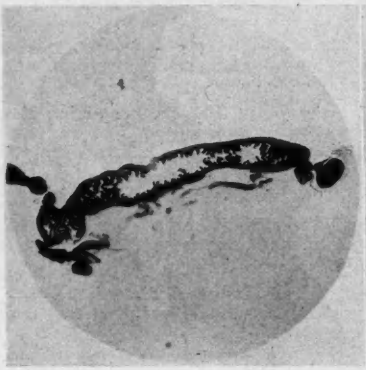
1. To 50 c.c. of first morning urine add 250 c.c. of 95 per cent alcohol. Shake and leave in refrigerator eighteen to twenty-four hours. A precipitate will form containing most of the hormone.
2. Pipette off the supernatant fluid, leaving about 100 c.c. containing the precipitate. Shake up precipitate in the remaining fluid. Pour into tube and centrifuge for about five minutes. Pour off the alcohol.
3. To the precipitate add 15 or 20 c.c. of ether and stir for about five minutes. Pour into tube and centrifuge for three minutes. Pour off the ether.
4. Dry precipitate with warm air. To this powder add 10 c.c. of sterile normal saline solution. After shaking well for a few minutes the first injection may be given at once.
5. Leave in refrigerator over night. Centrifuge again and discard the precipitate. The hormone is now in solution and ready for further use. It is relatively stable if kept in the refrigerator.

may be cut on the microtome within three to four hours after necropsy.

Should the test with 0.2 or 0.4 c.c. of unaltered urine prove to be grossly positive, another series of four animals is used, all of the same litter. These are injected with graduated doses of urine diluted with saline solution so that injections equivalent to 0.025, 0.05, and 0.1 c.c. are made. Rarely has greater dilution been necessary in our cases. In case of negative tests in animals injected with 0.2 and 0.4 c.c. but positive with 0.8 and 1 c.c., a similar group of four animals is used, three of which are injected with 0.3, 0.5, and 0.6 c.c. and one used as a control. In case all of the original animals were negative grossly, the hormone is extracted from the urine by Zondek's alcohol precipitation method (Table III). This technic is not infallible and many times the greater portion of the hormone is lost. We are now trying a new precipitation method, hoping to find a more satisfactory technic for concentration. A

similar plan of injections is carried out on these animals, but it rarely necessitates the injection of more than 0.4 c.c. Usually 0.2, 0.3 and 0.4 c.c. are the quantities injected.

The unit at present is at best on relative terms. To speak of 113 mouse or rat units would be presumptuous. In the light of our experience, one would be more nearly correct to say, probably between 100 and 300 mouse or rat units per liter of urine, rather than a set figure, especially if not in round numbers. We wish to emphasize that there are many variable factors in carrying out these



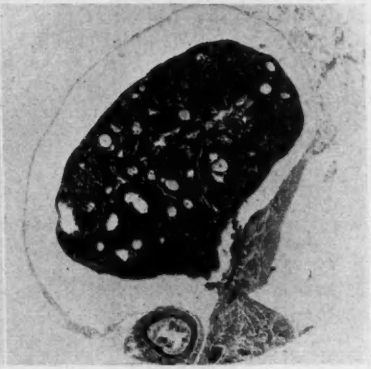


Fig. 8 (*left*). Enlarged uterine horn of infantile mouse in the absence of follicle-stimulating effect.

Fig. 9 (*right*). Mouse ovary showing absence of follicle-stimulating effects in the presence of extremely enlarged, edematous and colorless uterine horns.

tests. Five animals, all of the same litter and injected with the same doses of an identical urine, behave differently in a large number of cases. Some system of units, of course, has to be adopted. One can at least judge whether the quantity of hormone is high, moderate, low or absent. We have estimated the hormone on the basis of ripening of ovarian follicles or pronounced enlargement of the uterine horns. There have been many cases in which the ovarian follicles of the infantile mice were not stimulated but the tremendous enlargement of the uterine horns established the presence of the gonadtropic hormone (Figs. 8, 9). In case of hemorrhagic follicles and luteinization, which have been uncommon in our experience, the hormone is estimated in terms of luteinizing hor-

mone, rather than by multiplying the follicle-stimulating units by five, as does Ferguson. We are of the opinion that there are probably two factors present in the urine that bring about these reactions, but whether there are in fact two different hormones, as Zondek believed to be present in the urine of pregnancy, we, of course, at present do not know. Hamburger showed that, even of pregnancy, there is no constant factor between the follicle-stimulating dose and that of the luteinizing dose.

The mouse unit may be defined, then, as the smallest dose measured in cubic centimeters which produces definite ripening of the

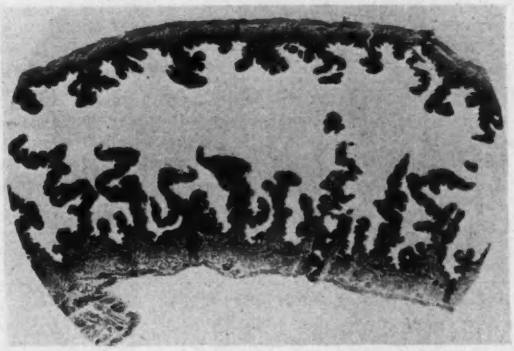


Fig. 10. Uterine horn (mouse) showing pronounced dilatation.

ovarian follicles or unmistakable enlargement of the uterine horns in the infantile mouse, when the injections are given five times in forty-eight hours and the animal killed in 100 hours. This unit divided into 1000 will give the number of units per liter of urine (Table IV).

We have injected much larger quantities of urine than that reported by other investigators. We began this practice purely by accident. Contrary to our expecations and reports by others, we found the infantile animals tolerated the larger doses equally well as the smaller ones. We do not lose many animals except in case of toxic urines, and in those cases the mortality rate among those receiving small injections is as high as among those receiving large

doses. It may be thought that, even if the animals did not die, such large doses might overload their circulation so as to prevent the physiologic reactions to proceed as normally as with smaller doses. This, however, does not prove to be true. Numerous tests have been positive when the animal received 1 c.c. at a single injection and negative when smaller doses were given. The main disadvantage of the larger dose is that there is more likely to be leakage

TABLE IV. MOUSE OR RAT UNITS OF TESTICULAR NEOPLASTIC HORMONE PER LITER OF URINE

Unaltered Urine

Amount	Number of Injections	Total Equivalent	Reaction	Units per Liter	
.025	5	.125	Definite ripening	8000	In case of corpora
.05	5	.25	of ovarian follicles	4000	lutea (Atretic) (R.
.1	5	.5	(R. I. Zondek) or	2000	II and III, Zon-
.2	5	1.	in case of refrac-	1000	dek) the units are
.3	5	1.5	tory ovaries, Pro-	700	the same but spok-
.4	5	2.	nounced enlarge-	500	en of as luteinizing
.5	5	2.5	ment of uterine	400	hormone.
.6	5	3.	horns.	300	
.8	5	4.		250	
1.	5	5.		200	

Concentrated Urine to One-fifth Original Volume

.2	5	5.		200	
.3	5	7.5		150	
.4	5	10.		100	
.5	5	12.5		80	
.6	5	15.		60	
.8	5	20.		50	
1.	5	25.		40	

from the opening made by the entrance of the needle. This is overcome, however, by selecting different sites for each injection and by using an extremely small hypodermic needle. There would be perhaps less excuse for using such large doses if it were not true that the present methods of concentration are inadequate. Our results with the Zondek technic of extraction conform with those of Hamburger, in that by this method only about 50 to 75 per cent of the original hormone is precipitated generally. Sometimes it appears that all the hormone is precipitated while at other times it is entirely lost. Many of our unaltered urine tests were positive but extraction was carried out with negative results.

THE EXCRETION OF HORMONE IN RELATION TO RADIOSENSITIVITY, PROGNOSIS, AND THE HISTOLOGIC STRUCTURE OF THE TUMOR

Our series of cases in which the hormonal excretions have been followed for sufficient length of time is too small to permit any definite conclusions regarding the relation of the quantitative hormonal studies to the radiosensitivity and the histologic structure of the tumors. It appears from our limited experience, however, that the hormonal excretion may be an important determining factor in the study of the relative radiosensitivity of the testicular tumors. Based on the reported studies in other clinics, in particular that of Dr. R. S. Ferguson at the Memorial Hospital with a series of thirty-seven cases, in which the histologic structure was verified, it would appear conclusive that this is the case. We are convinced, from a similar study of thirty-three cases, that there are several other important factors in addition to the hormonal behavior following irradiation which must be evaluated carefully.

In our clinic the mixed cell tumors containing adult tissues have proved to be relatively radioresistant. In tumors of this type which we have had the opportunity to observe, the hormonal excretion following adequate irradiation, has on several occasions indicated radiosensitivity on the basis of the pronounced fall or disappearance of the hormone. However, metastases have occurred, in spite of the low hormonal excretion, in a relatively short period of time. This may be interpreted on the basis of the known pathologic lesion to mean that the embryonal tissue, which was largely responsible for the excretion of the hormone, was definitely radiosensitive. Its destruction by radiation caused a pronounced decrease in the hormone. The adult tissue, however, which was not sensitive continued to spread by metastases in spite of irradiation (Chart 1). In the case of a mixed tumor of this type the diminution in hormonal excretion following irradiation does not indicate a good prognosis. One can expect the appearance of metastases. In our cases of embryonal tumors which were radioresistant the hormonal excretion increased considerably or clinical evidence of metastases became manifest within a period of from two to three months (Chart 2). Tumors composed largely of adult tissue with evidence of malignant differentiation caused low excretion of hormone in the urine and these patients, even when the hormone was

TABLE V. FACTORS IN DETERMINING RADIOSENSITIVITY OF TUMORS OF THE TESTIS

Testicular neoplastic hormone before treatment	High	Moderate	Low
Decrease following adequate x-ray therapy	Pronounced +30	Moderate +10	Slight -30
Histologic structure	Embryonal and unicellular +50	Mixed embryonal and adult +25	Adult +5
Rate of tumor growth as indicated by present status of patient	Within 2 months following treatment	Within 1 year following treatment	Within 2 years following treatment
Apparently well No. 1	+10	+30	+60
Apparently well but with T. N. hormone in the urine No. 2	-15	-5	0
Clinical evidence of metastases No. 3	-40	-20	-10
Individual	Normal 0	Anemic -10	Cachectic -40

absent following irradiation, showed metastasis usually within one or two years. The histologic structure and clinical experience are equally important in determining the prognosis.

The rate of growth of the tumor, when it can be determined clinically, runs closely parallel to its radiosensitivity. The rate of increase in the amount of hormone also aids materially in ascertaining this rate of growth.

There is an additional factor of importance in the study of these tumors which is difficult to evaluate. Some patients do not follow the above rules regarding radiosensitivity and prognosis. There is an individual factor which is related to the patient's physical condition. Ewing has mentioned this and has pointed out that if the patient is anemic or cachectic it may detract considerably from the expected results following adequate x-ray therapy.

Several factors must be considered in determining the radiosensibility of testicular neoplasms, namely, the histologic structure

of the tumor, the rate of growth of the tumor, the effect of irradiation on the growth and hormone and the physical condition of the patient.

These considerations have been outlined in Table V, which is presented, not with the idea of exact determination of the radiosensitivity of these tumors or the prognosis of these patients, but to illustrate the importance of studying each patient individually. Only in extremely small groups of cases selected from a large series

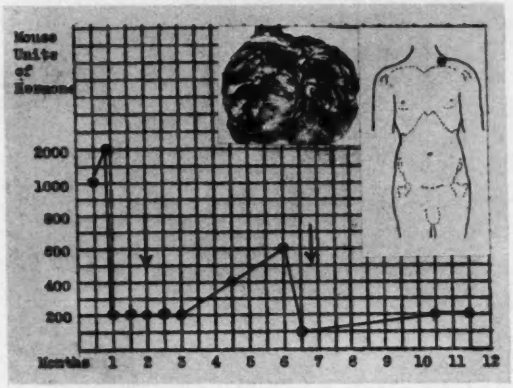


Chart 1. Graph showing the quantitative hormonal behavior in the case of an embryoid teratoma with malignant differentiation. There was a pronounced fall in the hormone to a level consistent with clinical cure, but metastases occurred within one year in spite of adequate irradiation. (Arrows indicate time of irradiation.)

can one obtain sufficiently similar factors to warrant any very dogmatic conclusions regarding either longevity in the case of the patient with any particular type of treatment, or to anticipate the behavior of the neoplasm itself. One of the most variable factors is the histologic structure of the tumor. A satisfactory classification of these tumors is wanting. Some tumors cannot be classified even by our most eminent pathologists. The hormonal test of the patient's urine may aid in the pathologic classification of some of the more uncommon testicular tumors.

Irradiation has varied considerably in this clinic. The earlier pa-

tients received inadequate therapy because of poor equipment, but the patients treated after 1928 under the direction of Dr. R. S. Stone have received what we believe to be adequate treatment, using the 200 Kv. equipment. A new high voltage roentgen-ray equipment has been installed which operates at potentials of 600 Kv. or higher.*

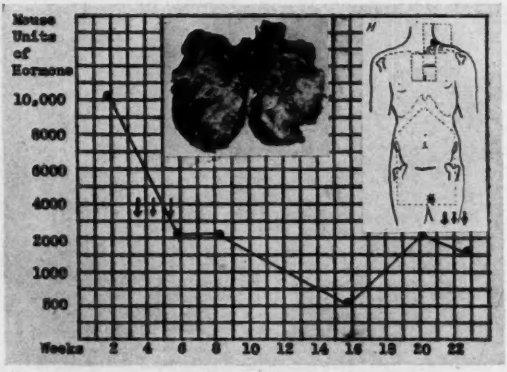


Chart 2. Hormonal chart of patient with an embryonal tumor with adult features. Note pronounced fall in the hormonal excretion following irradiation (indicated by arrows). Metastases occurred in the left supraclavicular area three months later in spite of this treatment.

The four cases presented in Charts 1, 2, 3 and 4 illustrate the main considerations which have been presented.†

SUMMARY

A. The Biologic Nature of the Hormone:

1. The pituitary gland, pregnancy and embryonal tumors are known causes of the appearance in the urine of gonad-stimulating hormones.

2. The stimulation of growth of gonad and genitals of infantile

*This equipment compares favorably with that of the Kellogg Radiation Laboratory at the California Institute of Technology at Pasadena. Drs. S. G. Mudd and C. K. Emery of that institution have treated a number of patients with heavily filtered irradiation at 850Kv. and have permitted us to follow this series with hormonal tests. We wish to acknowledge our great indebtedness for this privilege.

†A detailed analysis of cases will be presented later.

animals varies with the origin of the hormone producing it, the amount present in the urine and the animal used for the injections.

B. Technical Considerations:

1. Infantile mice and rats are used.

2. A qualitative test for as low as 250 units is made first on fresh unaltered morning urine. If positive, a quantitative test can be made.

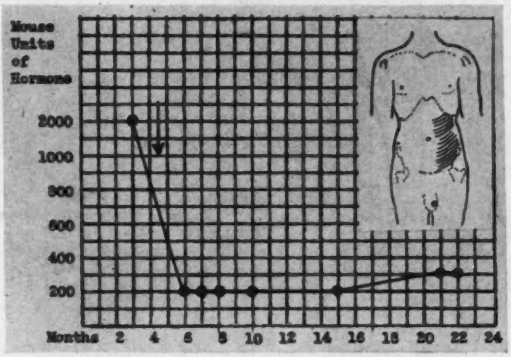


Chart 3. This graph represents an interesting patient with an embryonal carcinoma with lymphoid stroma. The patient lived seven years following simple orchidectomy without any irradiation before clinical evidence of metastases occurred. A large mass in the left side of the abdomen disappeared following a course of irradiation. The patient gained 40 pounds in weight and has worked one year since and is in perfect physical condition. The hormonal excretion of 2,000 units per liter of urine before irradiation is now 300 units per liter of urine.

3. The microscopic ripening of graafian follicles is more easily read in mice than in rats. The gross enlargement of the uterine horns is more definite in rats than in mice. At the age of twenty or twenty-one days the ovary of the rat may show open follicles normally. The Friedman test (rabbits) is unsatisfactory.

4. The hydrocele fluid with tumor of the testis contains more of the hormone than the patient's urine.

C. The Interpretation of the Tests:

1. The majority of tumors of the testis are embryonal and the

urine of these patients contains a substance which produces gross enlargement of the uterine horns or microscopic ripening of ovarian follicles (Reaction I of Zondek) when injected into infantile female mice and rats.

2. The presence of such a gonadotropic hormone in the urine of a patient with a tumor of the testis is presumptive evidence of tes-

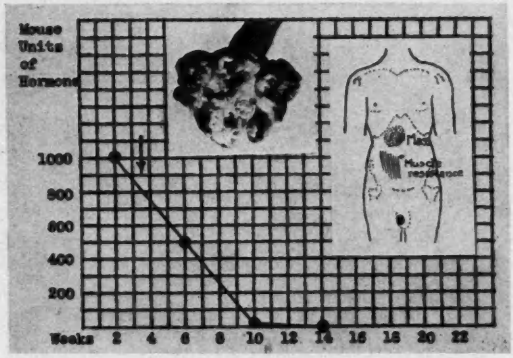


Chart 4. The tumor in this case is of particular interest. It was composed of two parts. The small portion near the rete testis was teratoid, containing cartilage and mixed tissues. About 1 cm. distant was a large mass composed entirely of embryonal adenocarcinoma. A palpable mass in the epigastrium disappeared under irradiation. Within two weeks the hormone had diminished from 1,000 units to 500, and within eight weeks to 100. (Arrow indicates time of irradiation.)

ticular malignancy and its absence is strong but not definite evidence against malignancy.

3. The effect of irradiation upon the amount of hormone in the urine, as determined by quantitative methods before and after radiation, gives a good indication of radiosensitivity, and may be used as a therapeutic test; in conjunction with the clinical effect on metastases, when present.

4. The therapeutic test of irradiation must be interpreted in conjunction with the histologic structure of the tumor, the clinical absence of metastases or the character of metastases when present and the physical condition of the patient.

5. The hormonal test, correlated as above, permits a more ac-

curate prognosis and a better control of therapy than has been possible heretofore, and may be of value in the classification of tumors the nature of which is in doubt on histologic study alone.

REFERENCES

COLLIP, J. B., THOMSON, D. L., MCPHAIL, M. K., and WILLIAMSON, J. E.: Anterior-pituitary-like hormone of human placenta. Canad. Med. Assn. Jour., 24:201, 1931.
(Fluhmann, D. F.: Proc. Soc. Exper. Biol. & Med., 29:1193, 1932.)

ENGLE, E. T.: Ovarian responses. Differences elicited by treatment with urine from pregnant women and by freshly implanted anterior lobe. Jour. Am. Med. Assn., 93:276, 1929.

EVANS, H. M., MEYER, K., and SIMPSON, M. E.: Relation of Prolan to the anterior hypophyseal hormones. Proc. Soc. Exper. Biol. and Med., 28:845, 1931.

EVANS, H. M., and SIMPSON, M. E.: A comparison of anterior hypophyseal implants from normal and gonadectomized animals with reference to their capacity to stimulate immature ovary. Amer. Jour. Physiol., 89:371, 1929.

IDEM: A comparison of the ovarian changes produced in immature animals by implants of hypophyseal tissue and hormone from the urine of pregnant women. Ibid., 89:381, 1929.

EWING, JAMES: Radiosensitivity. Radiology, 13:313, 1929.

IDEM: Factors determining radioresistance in tumors. Ibid., 14:186, 1930.

FERGUSON, R. S.: Quantitative behavior of Prolan A in teratoma testis. Amer. Jour. Cancer, 18:269, 1933.

FERGUSON, R. S., DOWNES, H. R., ELLIS, E., and NICHOLSON, M. E.: Preliminary note on a new method of differentiating the testicular tumors by biological means. Amer. Jour. Cancer., 15:835, 1931.

FLUHMANN, C. F.: Anterior pituitary hormone in the blood of women with ovarian deficiency. Jour. Amer. Med. Assn., 93:672, 1929.

HAMBURGER, C.: Hypofyseforlaphormon i Urinen fra mandlige Kastrater. Ugesk. f. laeger., 93:27, 1931.

IDEM: Sur la différence entre le Prolan A, provenant de Femmes enceintes et de castrats. Compt. rend. Soc. de biol., 112:99, 1933.

IDEM: Studies on gonadotropic hormones from the hypophysis and chorionic tissue with special reference to their differences. Acta Path. et Microbiologica Scand. Supplementum XVII, Copenhagen, 1933.

HARRIS, M. H., and BRAND, ERWIN: The existence of a monthly sex cycle in the human male. Science, 79:366, No. 2051 (April 20), 1934.

HILL, M., and PARKES, A. S.: The relation between anterior pituitary body and gonads. III. Fractionation and dilution of ovary-stimulating extracts. Proc. Roy. Soc., London, s. B., 107:455, 1931.

MAHNERT, A.: Über die Wirkung des Vorderlappenhormons (Prolan) auf die Ovarien infantiler Nager. Zentralbl. f. Gynäk., 54:1730, 1930.

ZONDEK, B.: Über die Hormone des Hypophysenvorderlappens. I. Wachstumshormon, Follikelreifungshormon (Prolan A), Luteinisierungshormon (Prolan B), Stoffwechelshormon? Klin. Wchnschr., 9:245, 1930.

IDEM: Über die Hormone des Hypophysenvorderlappens. II. Follikelreifungshormon, Klimakterium, Kastration. Ibid., 9:393, 1930.

IDEM: Maligne Hodentumoren und Hypophysenvorderlappenhormone. Hormonale Diagnostik aus Harn, Hydrocelenflüssigkeit und Tumorgewebe. Ibid., 11:274, 1932.

IDEM: Versuch einer biologischen (hormonalen) diagnostik beim malignen Hodentumor. Der Chirug., 2:1072-1073, 1930.

THE PROGNOSIS AND TREATMENT OF TUMORS OF THE TESTIS

FRANK HINMAN, M.D., F.A.C.S.
San Francisco

The purpose of this paper is to discuss prognosis and treatment of tumors of the testis, in the light of recent advances. Heretofore patients with such tumors have formed a particularly hopeless group in urology, and one in which there has been no uniformity or agreement in treatment. Recently a more hopeful attitude has appeared, inspired mainly by the advent of more powerful means and methods of irradiation. The majority of malignant tumors of the testis are embryonal in origin and such tumors are peculiarly radiosensitive. Almost everyone here has witnessed the remarkable clinical disappearance of extensive metastases under x-ray, and the construction of machines with which more massive irradiation is possible widens the sphere and the possibilities of such treatment. Along with this improvement in the method of treatment has come a means of diagnosis and control which is entirely new. This gives the ability to determine the presence of metastases before they make their clinical appearance and to detect any hidden resistant portion of large extensive metastases which clinically have disappeared entirely under x-ray therapy. It offers the opportunity of knowing more about the cause of the great variability in reaction to x-rays of tumors of the testis, which knowledge will permit a fairly accurate prediction of radiosensitivity. All these benefits of diagnosis and control of treatment are possible simply by testing the urine of patients for a gonad-stimulating hormone.*

The Three Considerations.—In consequence of these advances the prognosis and treatment of a tumor of the testis may be determined by the following three considerations and lines of procedure:

I. The diagnosis.
   1. The amount of the hormone in the urine before castration.
   2. Pathologic classification of the tumor after removal.

*See "The Gonadotropic Hormone in the Urine of Men with Tumor of the Testis, by Frank Hinman and Tracy O. Powell, preceding this article."

II. Metastases.
    1. The clinical evidence.
    2. The biologic evidence (the amount of hormone which persists up to two weeks after castration).

III. Radiosensitivity.
    1. Structural evidence.
    2. Therapeutic test of irradiation.
        a. Clinical effect (on metastases).
        b. Biologic effect (on hormone).

The first step in the problem of treatment is an early and a definite diagnosis. The hormonal test, in the short period of its application, seems to indicate with accuracy the presence or absence of testicular malignancy. However, it is not entirely specific. A positive test may be caused by the pituitary hormone, increased because of gonadal deficiency such as occurs with bilateral castration, or cyclically in normal men, or may be caused by an embryonal tumor elsewhere than in the testis. A negative test is good, though not positive, evidence that there is no testicular malignancy. A pure seminoma may not cause the excretion of the hormone. A number of negative tests have been reported.

The diagnosis can be determined definitely by histologic examination after castration. There can be no objection to simple castration, and a study of histologic structure is necessary to prognosis and the control of treatment.

Until recently all testicular tumors were regarded clinically as similar, always malignant and with the same route of metastasis. Greater experience with radiation, however, demonstrates a marked variability in the sensitivity of these various growths, and the newly applied hormonal test shows a great difference in the amount of hormone excreted in the urine of patients with different types of malignant tumors. The correlation of structure with the amount of hormone excreted, therefore, is of real value as the first step in the problem of treatment.

The second step is the determination of the absence or presence of metastases by clinical examination and the biologic test. For practical purposes patients can be divided into two groups: (1) Those without metastases; (2) those with metastases. The advantage of the hormonal test in the control of treatment is shown here. Patients who have no metastasis fail to excrete the hormone within two weeks after castration. When the hormone persists,

though reduced in quantity, in all probability metastases are present even though they cannot be demonstrated clinically. However, metastases may be so early and small as to produce insufficient hormone for the test. A negative test, therefore, is not evidence of cure. In the patient with clinical evidence of metastases, the amount of hormone excreted will be little affected by castration. The second step, therefore, in the determination of prognosis and treatment is the consideration of the clinical evidence for or against metastases and the effect of castration upon the amount of hormone excreted, in conjunction with histologic structure.

The third step is the consideration of radiosensitivity. This can be predicted by past experience with similar tumors and clinically tested by watching the effect of irradiation upon metastases when present and upon the amount of hormone in the urine. The determination of this sensitivity may be called the therapeutic test of irradiation. Three to four thousand "r" units to each field, requiring a period of three weeks for administration, will show by the effect clinically upon metastases, when present, and biologically upon the amount of hormone excreted one to two weeks later, the relative degree of radiosensitivity. The hormonal reaction indicates radiosensitivity more definitely than has been possible heretofore by a study of structure alone. In mixed tumors, however, the more rapidly growing and major portion of the tumor may be radiosensitive and disappear under x-ray while a small portion, which is highly resistant and malignant, remains. It is only by careful correlation of structure with the results of irradiation as shown clinically and biologically for long periods that a better understanding of variability will be reached.

On the basis of these three considerations—namely: diagnosis, metastases and radiosensitivity—patients may be divided for purposes of treatment and prognosis into two groups.

Group I contains those patients without clinical evidence of metastases, and in good physical condition; these can be subdivided by the result of a hormonal test, two weeks after castration, into a negative sub-group and a positive sub-group. The negative subgroup includes the few patients cured by castration. All of these patients, however, are not cured and should receive a hormonal test every three to six months for two years or longer. Reappearance of the hormone in the urine indicates metastasis. Should the mi-

croscopic structure of the tumor be similar to that which experience has shown is highly radioresistant, early radical removal of the pre-aortic lymph zone should be considered, irrespective of the effect of castration upon the hormone. The disappearance of the hormone after castration is only relative evidence of cure, for metastases may not produce sufficient hormone in the urine to give a test.

The positive sub-group includes patients with metastases so early or so limited as to give no evidence clinically. Limitation to the pre-aortic lymph zone gives the possibility of surgical removal and cure which should be attempted except for those growths highly sensitive to x-ray, as indicated by histologic structure and subsequently confirmed by the marked diminution or disappearance of the hormone after a therapeutic dose of irradiation.

Group II contains patients with clinical evidence of metastases. Castration may be indicated for local relief, but is in order mainly for diagnosis. Experience has shown that these patients are inoperable and that irradiation is the only curative treatment. The prognosis depends on the extent and rapidity of growth of the metastases and the general physical condition of the patient as well as the type of tumor and its radiosensitivity. The condition of the anemic, cachectic patient with extensive metastases, even though the tumor is radiosensitive, is almost as hopeless as that of the man with a resistant growth.

Summary of Prognosis.—These studies permit a fairly accurate forecast of the probable course of a patient. The chance of recovery may be estimated as (1) good, (2) fair, and (3) poor. In (1) the patient is physically fit, there are no demonstrable metastases and the hormone has disappeared from the urine. In (2), the patient is in good physical condition and the structure of the tumor indicates that it will respond well to x-ray therapy. However, metastases have appeared and the hormone persists even though low and diminishing under irradiation. In (3), the patient is losing ground physically, metastases resist treatment or rapidly recur and the hormone in the urine is little affected or even increases. Obviously the prospect of a patient may change. Any prognosis is tentative, but is of value in the control of treatment.

Summary of Treatment.—The division of patients into the two groups, those with and those without clinical evidence of metasta-

ses, is of value chiefly to the surgeon who believes he can accomplish anything by radical operation. An attempt to remove the regional lymph zone is justifiable only in patients in good physical condition and without any clinical evidence of metastasis. By how much will the radical operation improve the prognosis, which has been determined by the three steps outlined above, particularly by the correlation of histologic structure with the effect of castration and possibly the therapeutic test of irradiation upon hormonal excretion? The choice of radical operation is permissible for patients with a radioresistant type of tumor, but not for those with the radiosensitive type. The problem may be summarized briefly as follows:

GROUP I.

PATIENTS WITHOUT CLINICAL EVIDENCE OF METASTASIS, IN GOOD PHYSICAL CONDITION

A. The gonadotropic hormone disappears within two weeks after castration.
   1. Structure indicates radiosensitivity. (Prognosis good.)
   2. Structure indicates radioresistance. (Prognosis fair.)

B. The gonadotropic hormone is still present in the urine two weeks after castration. The therapeutic test by irradiation.
   1. Causes its diminution or disappearance, which indicates radiosensitivity. (Prognosis fair.)
   2. Has little or no effect on the amount of hormone excreted, which indicates radioresistance. (Prognosis poor.)

Treatment: Choice of radical surgery in A-2 and B-2.

GROUP II.

PATIENTS WITH CLINICAL EVIDENCE OF METASTASES

A. In good physical condition.
   1. Radiosensitive (metastases and hormone diminish or disappear under radiation). (Prognosis fair.)
   2. Radioresistant. (Prognosis poor.)

B. Anemic or cachectic (usually hopeless irrespective of the type of tumor).

Treatment: Irradiation.

Analysis of Fifty-four Patients.—The application of the foregoing considerations may be illustrated by a brief summary of personal experience. A more complete report of patients, with details of hormonal reactions, is planned in collaboration with Tracy Powell. The present incomplete analysis will serve as an example of the benefits which may be expected from more powerful inten-

sive radiation under the scientific control of the new biologic test.

The place of radical surgery in the treatment of tumors of the testis still remains, in most minds, one of theory and not of fact. Anything short of complete, clean removal of the primary and immediate secondary lymph zone is not radical. Whether this ever is possible can be proved only by trial. My own experience leads me to believe that it can be accomplished on the right side, but not on the left, on account of the superior mesenteric artery (Fig. 1). It might be possible, however, to remove the lymph zone of the left testicle which lies along the aorta, from the right side, which would leave the glandular area along the left iliacs. Modification of the abdominal incision on the right to permit the exposure of this area on the left, or a second short incision on the left side for this purpose might be considered in cases of tumor of the left testicle. It is, therefore, a question whether an attempt to remove the pre-aortic zone should not always be made from the right side irrespective of which testicle is involved.

Metastases occur in much the same manner in all varieties of tumor. Each testicle has its own primary set of glands which intercommunicate and also receive lymph from other structures. The number and arrangement of each set varies so much that the general distribution rather than any particular arrangement is of clinical importance. The primary set anastomoses freely through efferent vessels with an immediate secondary set. Invasion of the primary set on the opposite side and the immediate secondary set of both sides may occur early. Tumor cells may be carried in the blood stream to the viscera, usually the lungs and the liver, and when this has occurred operation is useless. The operation, therefore, should attempt the removal of all the lymphatics of the general distribution of the right and left primary and immediate secondary sets of glands. This generalized area has been clearly determined (Most, 1899; Cuneo, 1901; Jamieson and Dobson, 1910). It may be bounded (Fig. 1) by an imaginary transverse line from 1 to 2 cm. above the renal pedicle, by vertical lines extending from this point on each side just outside the vena cava on the right and from 1 to 2 cm. outside the aorta on the left to the level of their bifurcation, then following along the iliacs to cross at the upper third of each external iliac, and following these vessels back to about 1 cm. below the bifurcation.

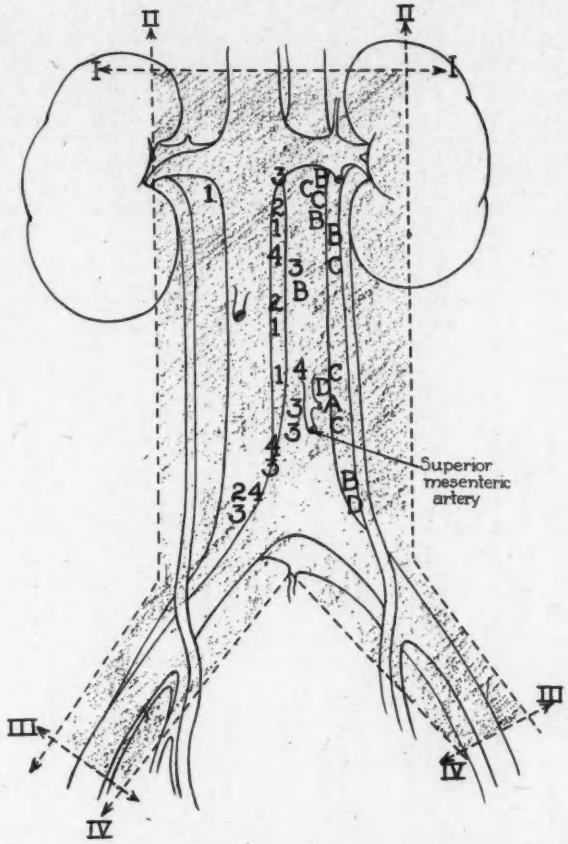


Fig. 1. The general distribution of the primary lymphatics of the testicle. I. Superior boundary. II. Lateral boundary. III and IV. Inferior boundary. *Right:* (1) Four primary lymph nodes; (2) Three primary lymph nodes; (3) Six primary lymph nodes; (4) Four primary lymph nodes. *Left:* (A) One primary lymph node (Specimen 7); (B) Five primary lymph nodes (Specimen 2); (C) Five primary lymph nodes (Specimen 4); (D) Two primary lymph nodes (Specimen 3).

(After actual dissections of Jamieson and Dobson, 1910.)

TABLE I. ANALYSIS OF FOURTEEN PATIENTS SUBJECTED TO RADICAL OPERATION

No.	Date of Radical Operation	Age and Location	Previous Duration	Structure	Glands	Recurrence	X-ray	Result
1	12-11-'17	33—R	1½ years	Teratoma	+			(1 yr. 1 mo.) Lost 1
2	1-29-'18	30—L	(Trauma 7 yrs.) 9 months	Teratoma	+			Living and well 14 years 1
3	7-23-'18	36—R	6 months	Teratoma	Extensive to one gland over aorta			(3 months) Lost 1
4	7-24-'18	34—R	4 months	Seminoma	Marked hyperplasia. Extensive to one gland between aorta and vena cava	To supra-renal glands		Died 4-6-'20
5	1- 4-'27	34—L	(Trauma 5 yrs.) 7 months	Teratoma	++	No	+	Living and well 10-19-'25 4 years. 10½ mos. 1 (lost)
6	6-30-'22	30—R	6 months	Teratoma	Hyperplasia	To retroperi-toneal glands, liver, lungs	+	Died 5-22-'23 1 yr., 6 mos.

7	1-21-'24	24—R	6 months	Teratoma	No	No	No	Letter, 8-29-'32 Living and well 8 yrs., 9 mos. 1
8	1- 8-'25	25—R	5 months	Teratoma	Gland on renal pedicle	Virchow's and preaortic		6 weeks Died 3-23-'25
9	10-16-'26	66—R	1 year	Teratoma	No	No	No	Living and well 6-19-'29 2 yrs., 8 mos. 1
10	12-27-'29	32—L	2 months	Teratoma	Hyperplasia	No	No	Living and well 5-1-'34 5 yrs., 1 mo. 1
11	1-18-'33	27—L	5 months	Chorion-epithelioma	Glands over aorta	Yes	+	Died 5-4-'34 + 5000
12	1- 6-'33	34—L	2½ years	Seminoma	No	No	+	Living and well 1 yr., 4 mos. 5-2-'34 —50 1
13	4-31-'26	35—R	2 months	Teratoma	No	No	+	Living and well 1 yr. —50 1
14	6-23-'33	23—R	3 months	Teratoma	No	No	+	Living and well 1 yr. 1

The accompanying three tables give a brief analysis of twenty-five patients without clinical evidence of metastases when first seen, and of twenty-nine patients with clinical evidence of metastases. The term teratoma designates a mixed type of malignant tumor, and seminoma, the homogeneous type composed of large polygonal cells which resemble a spermatocyte. At present confusion in terminology is inevitable. This is well illustrated by the following attempt to classify the varieties which have been reported:

CLASSIFICATION OF TUMORS OF THE TESTIS

I. Homologous
   A. Benign
      1. Epithelial
         a. Adenoma of the seminal tubules
         b. Misplaced ectoderm
      2. Mesoblastic
         a. Interstitial cell tumors (probably not true tumors but merely hyperplasia [Ewing])
         b. Tumors of connective tissue
         c. Misplaced mesonephric tissue
   B. Malignant
      1. Epithelial
         a. *Seminoma* (unicellular)
      2. Mesoblastic
         a. Sarcoma (lymphosarcoma, myosarcoma)
      3. Tumors of adrenal rests (small cell adenocarcinoma derived from adrenal tubules, occurring in men of middle age and running a slow course [Ewing, Bell, Stevens])

II. Heterologous
   A. Benign
      1. Dermoid cysts (simple and complex)
      2. Organized embryomata
   B. Malignant (mixed cell tumor)
      1. Adult teratoma (with few or early malignant changes)
      2. *Malignant teratoma* (embryonal carcinoma) occurs as complex varieties of fairly uniform to very mixed tumors. Uniformity
         a. Hypoblastic (embryonal adenocarcinoma)
         b. Mesoblastic (embryonal carcinoma with lymphoid stroma)
         c. Epiblastic (basal cell epithelioma, neurocytoma, etc.)
         d. Trophoblastic (chorionepithelioma)

III. Tumors which cannot be classified.

TABLE II. ANALYSIS OF ELEVEN PATIENTS, WITHOUT CLINICAL EVIDENCE OF METASTASES, TREATED BY CASTRATION AND X-RAY

No.	Age and Location	Previous Duration	Structure	Appearance of Metastases	X-ray	Hormone	Results
1	R	6 months	Seminoma	Yes	++		Dead 2½ years
2	1¼—L	5 months	Teratoma Fibrosarcoma		No		Dead 6 months
3	40—R	3 months	Teratoma	Yes	? S.E.D.		Dead 1 year
4	35—R	?	Teratoma	7 years after orchidectomy	(Since app. of metast.) 3200	400	2
5	34—L	2 years	Seminoma	None in 7 years	+	1000	2 7 years
6	R		Teratoma	No	Adequate	250	2 1 year
7	22—R	3 months	Teratoma	No	Adequate	1000	2 3 years
8	L		Seminoma	No	+	Neg.	1 2 years
9	32—L	3 months	Teratoma	Virchow's removed 2 months	Adequate	2000	3 4 months
10	32—L	3 years	Teratoma	Yes	++	+	3 3½ years
11	35—L	3 months	Teratoma	Yes	Adequate ++	400	3

TABLE III. ANALYSIS OF TWENTY-NINE PATIENTS WITH CLINICAL EVIDENCE OF METASTASES WHEN FIRST SEEN

Case Number	Age and Location	Previous Duration	Structure	X-ray	Hormone		Result
(Dr. Harris, 1 1926)	Bilateral	Few mos.	Teratoma	Massive 1st in 1926; 2nd in 1930		First abdominal metastases appeared in 1930	Lived 8 yrs. Died (1933) of gastric ulcer
2 6854	22—L	2 years	Lympho-sarcoma	1000 *r* units (radium 167 mg. 18 hrs.)			Dead, 6 yrs. 2 mos.
3 16689	49—R	1 day	Sarcoma	None			Dead, 3 yrs.
4 54159	32—R	3 years	Teratoma				Dead, 3 yrs.
5 69007	28—R	2 years	Seminoma	S.E.D.			Dead, 2 yrs.
6 68453	43—L	2 years	Teratoma	Massive			Dead, 2 yrs.
7 21378	45—R	3 years	Seminoma	400			Dead, 1 years
8 A.B.	20—L	1 year	Teratoma	40,000			Dead, 1½ yrs.
9 B.C.	20—L	3 weeks	Teratoma	40,000	20,000		Dead, 1 year
10 C.D.	22—R	6 years	Teratoma	400	5,000	Abdominal Pulmonary	Dead, 1 year
11 33525	R			250	5,000 (before death		Dead, 9½ mos.
12 91348	38—R	3 months	Seminoma	3,400			Dead, 9½ mos.
13 61344	54—R	7 months	Teratoma	1,400			Dead, 8 mos.
14 20119	40—R	1 year	Seminoma	800			Dead, 5 mos.

15 12361	10—L	4 months	Seminoma	None			Dead, 4½ mos.
16 59797	43—R	3 months	Teratoma	800			Dead, 6 mos.
17 43389	59—R	5 months	Teratoma	None			Dead, 6 mos.
18 081312	21—R	1 month	Teratoma	None		Undescended testicle	Dead, 2 mos.
19 E.F.	29—R	?	Teratoma		200	Extensive metastases	Dead, ?
20 (P)	24—R	6 months	Seminoma	23,800	500		Living 5 yrs. 2
21 (P)	35—R	1 year	Seminoma	11,120	500		Living 1½ yrs. 2
22 (P)	L	?	Teratoma	None	1,000		Living 6 mos. 2
23 (Marine Hosp.)	21—R	1 month	Teratoma	1,600	+		2
24 41482	37—R	2 months	Teratoma	None		Lost 14 lbs. in hosp. Extensive metastases	Lost after discharge 3
25 48678	51—L	3 months	Seminoma	None		Metastases Extensive	Living 1 year 3
26 E.	52—R	13 months	Teratoma		500	Physical condition poor	Living 2 years 3
27 F.G.	34—L	2 years	Teratoma	40,000	3,000	Fell to 800 after x-ray	3
28 96598	25—R	2 years	Teratoma	1,200		Abdominal Lungs	3
29 (P)	32—L	3 years	Teratoma	Consider-able		Extensive	3

The foregoing classification is elaborate and may increase rather than diminish the present confusion. Structural characteristics of tumors of the testis are not always definite. Occasionally a growth is found which defies classification, and frequently structure raises points of reasonable disagreement. The new hormonal test will be of great assistance in settling many questions now in dispute.

For clinical purposes two clear-cut types of malignancy occur, the radiosensitive and the radioresistant. Relative sensitivity must be recognized, that is, the tumor of mixed type of which the more rapidly growing major portion is highly sensitive and the remaining smaller part resistant and malignant. Correlation of structure with sensitivity is not attempted in the present analysis.

Summary of Group I.—Of the twenty-five patients in Group I, with no evidence of metastases, fourteen have had radical operation (Table 1), nine for right-sided, and five for left-sided tumor. Ten are living, all with a good prognosis (no metastases, no hormone); four are dead.

Seven showed metastases in the glands removed at operation. Four of these are living: fourteen years, four years and ten months, one year and one month, and three months, respectively. Three are dead.

Seven had glands removed which did not show metastases. In two of these patients there was an unusual degree of endothelial hyperplasia and one is living and well six years and one month. The other is dead. The five others are now living: eight years nine months, two years eight months, one year four months, and the remaining two, one year, respectively.

Of the eleven patients without metastases, treated by castration and x-ray therapy (Table II), eight are living: one for two years, with a good prognosis; four with only a fair prognosis because the hormonal tests are positive; and three with a definitely poor prognosis (metastases have appeared and the amount of hormone in the urine has increased in spite of irradiation). Of the four patients with a fair prognosis, one lived seven years before metastases appeared, but now the amount of the hormone in the urine is increasing in spite of x-ray therapy; another has lived seven years since castration but, although metastases are not evident clinically, the amount of the hormone in the urine is increasing. The other two with a fair prognosis have lived one and three years respec-

tively without clinical metastases, but with positive hormonal tests.

Summary of Group II.—Of the twenty-nine patients in Group II (with clinical evidence of metastases when first seen, Table III) only ten are alive; four with a fair prognosis (radiosensitive—living five years, one and one-half years, six months and a few months respectively, all with positive hormonal tests) and six with a poor prognosis (radioresistant). The case of one of the nineteen patients who died is rather remarkable and illustrates the marked radiosensitivity of some tumors. In 1926, this man developed bilateral teratomata within a few months and was given an inten-

TABLE IV

	Group I Patients Without Metastases		Group II Patients With Metastases
Treatment	Radical Operation	Castration and Radiation	
Number of Patients	14	11	29
Dead	3	3	19
After 4 years	None	1	2
Living	11	8	10
Prognosis 1	10	1	None
Prognosis 2	None	4	4
Prognosis 3	1	3	6
Over 4 years	4 (1)	1 (2)	1 (2)

sive course of x-ray therapy. The first evidence of abdominal metastases appeared in 1930 and disappeared promptly under a second course of treatment. He died in 1933 of gastric ulcer, eight years after castration, apparently without recurrence. Unfortunately there was no autopsy.

The comparative results in the foregoing three groups of patients may be summarized as shown in Table IV.

It is not intended to leave the reader with the impression that the author believes radical surgery so much superior to irradiation as this summary indicates. This is a very small series and the good results with surgery may be coincidental and not causative. The facts, however, that there have been no surgical deaths and that an occasional patient with a radioresistant type of tumor may be saved, sufficiently justify the operation whenever the right opportunity for it is presented.

DISCUSSION

DR. HOMER G. HAMER (Indianapolis, Ind.): I would like to report two unusual cases of malignant testicle. The first was a young man of thirty-four who last June noticed tenderness and hardening of his left testicle after a slight injury. He also observed tender and secreting breasts. On examination, the left testicle was found to be about one-half the size of its normal fellow, globular, hard and smooth. The Aschheim-Zondek reaction was positive. Orchidectomy was performed in September. The histologic diagnosis was teratoma testis. A course of x-ray treatment was given following operation. The Aschheim-Zondek reaction has remained negative. There is no evidence of recurrence or of metastasis. He is at present in good health.

The second case occurred in a young man of forty-four who in November noticed enlargement and soreness of his right testicle after a fall in which he thought the testicle was injured. Examination disclosed a nodular right testicle simulating tuberculous epididymitis. The Aschheim-Zondek was negative.

With the pre-operative diagnosis of chronic epididymitis simulating tuberculosis but possibly malignant, orchidectomy was performed in February last. At operation, after incision of the tunica vaginalis, unmistakable nodulation of the testicle was detected. The testicle was therefore removed. Histologic examination showed an adenocarcinoma of the testicle, the neoplastic cell characterized by a similarity to the spermatocyte. A course of x-ray treatment was given. The wound broke open and has shown no tendency to heal. Swelling and induration about the stump of the cord has developed. The Aschheim-Zondek reaction remains negative.

The first case is presented because of the small size of the involved testicle and the accompanying breast activity.

The second case is of interest because of the simulation of tuberculosis, the negative Aschheim-Zondek reaction and the radioresistant character of the tumor, which we believe to be of the rare type of malignancy, having its origin in the adult tubule cell described by Gordon and by Ewing and recently referred to by Fer-

guson as the type of tumor likely to give a negative Aschheim-Zondek reaction.

DR. F. H. HAGNER (Washington, D. C.): We have had three cases which we have studied by the Aschheim-Zondek test. I will mention these cases following those the doctor has described. In two of these patients the Aschheim-Zondek test showed positive reactions. The third patient showed a negative reaction and the diagnosis in this case proved to be a general fibrosis of the testicle; there was no evidence of malignancy. We have had one case which I think is rather unique and interesting. That was a patient on whom I did an orchidectomy nine years ago. At that time, of course, we did not have the powerful x-ray instruments we have at present, and he was given x-ray treatments before operation. He remained perfectly well for nine years. He then came to us with a tumor in the left side of his neck, and an Aschheim-Zondek test was positive. He was given massive doses of x-ray, and as his tumor promptly disappeared, the Aschheim-Zondek reaction became negative. He was perfectly well then for nearly a year, when he came to us with a retroperitoneal tumor in his mid-abdomen, about that size (indicating). He again had a positive Aschheim-Zondek reaction. Massive doses of x-ray were again given, the tumor disappeared, and the test again became negative. He has remained well for about six months. We went back and studied the original growth. It was a teratoma of embryonal type, and largely sarcomatous cells.

DR. TRACY POWELL (San Francisco, Calif.): I would like to show a few slides.

(Slide) Here is a large solid tumor of the testicle in a patient whose blood Wassermann reaction was positive. The hormonal tests on the patient's urine were negative. This illustrates the value of the hormonal tests occasionally in diagnosis. We have had three similar cases all giving negative hormonal tests. I understand, however, there has been reported a case of gumma of the testicle which gave positive hormonal tests.

(Slide) Eight years ago this patient was subjected to unilateral orchidectomy in another city. He received no roentgen therapy, but in spite of this lived seven years before clinical evidence of metas-

tases occurred. At that time a large mass could be palpated in his abdomen. Due to the surgical absence of a testicle we suspected metastatic tumor.

Quantitative studies on the patient's urine revealed the presence of about 2,000 mouse units of the gonadotropic hormone per liter of urine. When subjected to deep roentgen therapy the mass disappeared. The hormonal excretion decreased to around 200 mouse units per liter of urine and has remained low since.

One year has now elapsed, the patient has gained forty pounds in weight and works every day, apparently in excellent physical condition. This illustrates the value of deep x-ray therapy in cases of radiosensitive tumors. This case was that of an embryonal carcinoma.

(Slide) This graph is that of another interesting case of tumor of the testis. The patient's urine was found to contain about 1,000 units of the gonadotropic hormone per liter of urine. Following castration the tumor was found to be of the seminoma type, also referred to as embryonal carcinoma. It contained a lymphoid stroma. The hormonal excretion fell the following day after castration to about 100 units per liter. As we did not know how to interpret this low hormonal excretion a radical gland resection was carried out, but no metastases were found. In spite of adequate irradiation, however, the hormonal excretion has gradually increased, but is still below that which has been considered consistent with clinical cure. It will be interesting to learn if this low hormonal excretion does represent metastases.

(Slide) This man had an unusual type of tumor. When examined clinically it appeared to be an enlargement of the upper pole of the epididymis.

Quantitative studies on the patient's urine indicated the presence of about 1,000 units of the gonadotropic hormone per liter. Following orchidectomy the pathologic specimen was of particular interest. There was a small tumor about the size of a pea near the rete testis which was definitely a mixed cell tumor. It contained cartilage and several other types of tissues. At the uppermost portion of the testicle near the periphery there was a much larger tumor, composed entirely of embryonal adenocarcinoma.

This specimen supports Dr. Ewing's theory regarding the histopathologic origin of the testicular tumors. A large mass felt in the

patient's abdomen disappeared following irradiation, and the gonadotropic hormone could not be detected in the urine.

(Slide) This man had a tumor similar to the case of seminoma I mentioned before, with only about 500 units of the hormone in his urine, but, in spite of adequate irradiation persistently carried out, his hormonal output became increasingly higher and he died with generalized metastases in a short period of time.

(Slide) This is an unusual case in that it is a chorionepithelioma, the type of tumor which causes large quantities of the hormone to be excreted in the urine. This man, in spite of irradiation, developed metastases and has been going down rather rapidly.

(Slide) This represents a patient with an adult type of cystic teratoma with malignant differentiation. He had about 1,000 units of the hormone in his urine before operation, which fell to about 200 units the day following orchidectomy. He developed metastases, which partially disappeared under x-ray. This again represents another case with low hormonal output, sufficiently low to be consistent with clinical cure, yet we know with 200 units this patient developed metastases with little or no increase of the hormone.

(Slide) This patient had already had an orchidectomy when he came to our clinic, and the tumor was of embryonal type, but was composed of all three germ layers. He had about 10,000 units of the hormone in his urine, but after considerable irradiation it fell to 2,000 units. Later the hormone decreased to 500 mouse units per liter, but rapidly increased again up to about 2,000 units, when he was given additional x-ray therapy. At the present time, however, he has about the same amount of hormone. This man had never had any hair on his chest until he developed this tumor, when it rapidly grew on his chest and he also became an over-sexed individual. It is interesting to know that in spite of the high excretion in this patient's urine this man has no hypertrophy of the prostate.

DR. ALEXANDER RANDALL (Philadelphia, Pa.): I would like to ask two or three questions. Dr. Powell refers to a reading of 200 mouse units as conducive to conclusion of clinical cure. Is there a normal content of hormone?

DR. POWELL: That was a point I was trying to bring out in one of these cases. Dr. Ferguson has referred to the fact that an

amount below 400 mouse units per liter of urine was consistent with clinical cure. Yet the patient I referred to developed metastases with as low as 200 units of the hormone in his urine.

DR. RANDALL: Does he mean that 400 mouse units per liter is a normal amount?

DR. POWELL: Of course, we haven't followed a sufficient number of cases long enough to know. It is assumed that there may be some hormone remaining in the blood or tissues even after the tumor is destroyed. I firmly believe that perhaps at certain times there may be a gonadotropic hormone, such as the anterior pituitary, that may be confused in these low hormonal readings, but when the hormonic excretion is sufficiently high this element is ruled out. I personally do not know exactly what is normal. Theoretically, it is not normal to have any.

DR. RANDALL: Another question I want to ask Dr. Hinman. He refers casually to castration. Does he mean total or partial castration?

DR. HINMAN: I mean just removing the tumor and testicle.

MALIGNANT GROWTHS IN THE UNDESCENDED TESTIS

REVIEW OF THE LITERATURE, AND REPORT OF TWO CASES

DAVID W. MacKENZIE, M.D.

From the Department of Urology, Royal Victoria Hospital, Montreal

In a previous article on "Tumors of the Testis" (1931)[8] we reported our series of thirteen cases and briefly reviewed the literature up to that date. Discussing the etiology we emphasized the fact that we had not seen a case of malignancy in our series of 105 undescended testes. This observation, together with similar reports by other authors, led us to believe that undescended testes *per se* were not seriously predisposed to malignant degeneration.

Since 1931 we have had under our care twelve additional cases of tumor of the male sex gland; of these two were in undescended testes. We may add here that although we are reporting two such cases, yet we are still of the opinion that there is very little danger, if any, of malignant changes in undescended testes whether inguinal or abdominal.

There are several facts and clinical observations that influence us to support this view. In the first place there is really no definite proof to show that undescended testes are predisposed to malignant changes. The only arguments advanced are based on statistics, and we know that statistics very often contradict themselves. In reviewing the literature we find a variety of reports asserting that tumor formation occurs anywhere from thirty to three hundred times as often in the undescended as in the normally placed gonad. Similarly, there are differences of opinion regarding the relative frequency of malignancy in inguinal and abdominal cryptorchids. Some authors state that inguinal testes are more prone to develop malignancy; others have the opposite view. Recently Rea reported eleven cases of tumor in undescended testes; of these, six were in abdominal and five in inguinal cryptorchids.

The following are some of the reports that show rather high percentages. Deane reports that 13.5 per cent of all tumors of the testis were found in undescended organs. Hinman reviewed 649 cases of cancer of the gonads and found 12.2 per cent in unde-

scended testes. Rubaschow reviewed the cases of undescended testes reported by twenty-one observers, and found that in 11 per cent of the whole group tumors were present. This figure is a rather high one.

When, however, we come to other reports we see rather striking contrasts. Cunningham saw sixty-seven cases of tumor of the testis at the Boston City Hospital, without one being in an undescended testis. This observation, by the way, led Cunningham to conclude that "there does not seem to be anything in the condition of undescended testis *per se* favoring an earlier development of malignancy." Eccles reports 859 cases of undescended testes without finding malignancy in any of them. Coley did not have a single case of malignancy in 1,357 cases of undescended testes. Kocher found only one case of malignancy in 1,000 cases. Hinman states that one case of malignancy in an abdominal cryptorchid is found in every 60,000 admissions of undescended testes.

Very interesting and rather striking information is obtained from the medical records of the World War. These show that there had been 3.1 cases of undescended testes for every 1,000 men examined, that is 0.31 per cent. This observation is undoubtedly more accurate than other estimates (0.1 per cent, Marshall) since it was determined after the examination of thousands and thousands of men. This being the case, there must have been a very large number of men with undescended testes. Therefore, if the theory is correct that undescended testes are predisposed to malignancy, then there should have been many cases reported, but no mention of them is made.

There is another angle of the subject that is most interesting. The majority of growths of the undescended testes occur when sex life is most active, that is between twenty and forty years of age. If undescended testes are predisposed to malignant degeneration, why does not the change occur earlier in life—if not carcinomatous at least sarcomatous? That is not so, however. In our cases the ages were thirty and forty-eight years, respectively.

Finally, there are not many cases of tumor of undescended testis reported in the literature. Up to date and including our two patients, there are approximately 156 cases.

What is then the theory of the origin of the growths? We feel that they have the same origin as those of normally placed testes,

namely that there are aberrant sex cells present which have an inherent quality to form growths which resemble rudimentary fetuses, the so-called teratoma. These aberrant cells are omnipotent and when they start growing have the power to form every order of cell in the body (Adami).

A few words must be said regarding the so-called prophylactic treatment of undescended testes. There are some authors who, being very strong believers in the potential malignancy of undescended testes, advocate orchidectomy in every case. This procedure, to our way of thinking, is a most drastic one and not warranted when one considers that only one patient out of 60,000 cases of cryptorchid might develop malignancy of an abdominal testis. To emphasize their point they have recorded a case of cryptorchidism in which malignancy developed after orchidopexy (Lund). They use this to show that undescended testes are prone to develop malignancy after orchidopexy, and therefore orchidectomy is justified. This argument does not seem to justify their conclusions, since we have been able to find in the literature only one other similar case (Rea).

Pathology.—The pathology of growths of the testis is the same as that of normally placed testes. They are practically all malignant and may be divided into four groups.

1. Embryonal carcinomata or teratomata
2. Teratoid or mixed growths
3. Chorio-epithelioma
4. A miscellaneous histoid group, made up of dermoids, fibromata, chondromata and sarcomata

Symptomatology.—The symptoms of growths of cryptorchids are obviously different from those of normally placed testes, and depend on the site of the undescended organ. If the testis is in the inguinal region the patient usually complains of a mass in the groin with a sense of heaviness in that region. On the other hand, if the testis is in the abdomen there are no symptoms until late, when a mass in the abdomen manifests itself. Very often pain is complained of and may be quite severe, simulating an acute abdominal condition. Occasionally torsion occurs with rupture of a blood vessel and the signs are those of general peritonitis (Vastola).

Tumors of the testes, whether normally placed or undescended,

are very malignant and metastasize very early and extensively. As a result patients very often will first consult a physician for other conditions. For example, when the retroperitoneal glands become involved the patient seeks a doctor's advice for gastro-intestinal symptoms, and only after routine examination is the real state of affairs ascertained. The same may be true of the other systems of the body. We have in mind at the present time a patient who first consulted his physician for a cough. It was later discovered to be due to metastases of the lung secondary to a growth of the testis.

Diagnosis.—The diagnosis of malignancy of the undescended testis is usually not difficult. Here, too, however, one may encounter the same surgical conditions that affect the perfectly descended male sex gland. Tuberculosis, syphilis, hydrocele, hematocele and chronic torsion are to be ruled out. We must again emphasize that a positive Wassermann reaction does not definitely rule out a new growth. We have seen tertiary syphilis and a new growth of the testis co-exist. The safest and most reliable procedure is to use the so-called therapeutic test. If the mass is due to syphilis, it will reduce in size by anti-luetic therapy.

Treatment.—Our method of treatment of tumors of the testis, whether undescended or normally placed, has changed somewhat in the past few years. We first give a course of deep x-ray therapy. This is followed by orchidectomy and several courses of x-ray treatment over a very long period of time. We have our patients report periodically every two to three months for observation. Since using this new method our results appear to be more satisfactory; even those who first came with metastases seem to have improved. In a small number of our patients who showed metastases in the chest and retroperitoneal glands, the masses have entirely disappeared or have been reduced in size considerably after the course of deep x-ray treatment.

A word again about the treatment of undescended testes. We are strongly of the opinion that no case of cryptorchidism *per se* is to be subjected to orchidectomy.

The following is a résumé of our two cases:

Case 1.—M. S., aged thirty years, was admitted to the Department of Urology, Royal Victoria Hospital, on December 21, 1933, complaining of tender swelling in the left groin.

Following a herniotomy, right, twelve years ago in Germany, the wound became infected and an orchidectomy on that side had to be performed. The patient denied venereal disease. There had been no other serious illnesses except scarlet fever and measles in childhood.

Fig. 1. Case 1. Photograph showing an embryonal carcinoma in an undescended testis, which has been split open. The cord is shown attached.

The parents, two brothers and one sister are alive and well. No familial diseases were reported.

The patient stated that the left testis was never down in the scrotum, but has always been in the left groin. He was not troubled, however, until about two weeks prior to admission, when he noticed that the

mass in the left inguinal region was much larger in size, and that there was definite discomfort in that region. The discomfort gradually increased in severity, and for a week prior to admission the mass was quite tender.

Physical examination revealed a well developed and nourished white man, who appeared quite comfortable. The following points were noted: Head, no deformities; neck, no large lymph glands; eyes, pupils equal, react to light and accommodation; nose, some congestion of the mucous membrane; ears, normal; teeth in good condition; tongue, moist and clean; tonsils, enlarged, but not inflamed; thyroid, slight left lateral lobe enlargement.

The chest was symmetrical. Expansion was good and equal. Percussion note was clear. Breath sounds were easily heard and normal in quality. No râles were heard.

The pulse was regular, of good volume and tension. The vessel wall was not thickened. The heart was not enlarged to percussion and heart sounds were well heard at all areas. No murmurs were present. Blood pressure was 118/75.

The abdomen was well formed and moved well with respiration. There was an irregular swelling on the left side of the abdomen in the upper part of the inguinal region. It seemed to be right under the skin and was tender to palpation. There was a well healed scar in the right lower quadrant. Liver and spleen were not palpated. No other masses were felt. Flanks were clear.

Extremities were normal. Nervous system was normal.

There was no costolumbar tenderness in the kidneys. They were not palpated. There was no tenderness along the course of ureters and no suprapubic distention or tenderness of the bladder. The penis was normal. There was no discharge from the urethra.

There was a well healed scar on the right side of the scrotum. Neither the right nor left testis was present in the scrotum. In the left groin there was a movable irregular and rather tender mass the size of a plum. It did not seem to be in the inguinal canal. It was the left testis and appeared to be maldescended. We were unable to discern the epididymis from the testis.

The prostate was not enlarged or tender, and was not fixed. Seminal vesicles were not palpated.

Laboratory Data

Urinalysis: (voided)
Hazy straw, acid, 1018 (W.B.C. rare. R.B.C. none seen.
Albumin none, sugar none (Epith. cells. Amorph. urates +.
1 c.c. Phthalein intramuscularly:
First hour 55 per cent
Second hour 15 per cent. Total 70 per cent.

Blood Count:	Red blood cells	5,480,000
	White blood cells	8,200
	Hemoglobin	85 per cent

Pre-operative diagnosis was tumor of the testis, left, maldescended.

Operation for malignant growth of maldescended left testis was performed December 23, and consisted of a left orchidectomy using gas and ether anesthesia. A left inguinal incision was made. A large irregular testis was found beneath the external oblique opposite to the internal ring. The cord was freed and delivered. It was quite long and was carefully examined on account of nodular contour and variation in consistency. It was thought advisable to remove this en masse to the internal ring, and follow with deep x-ray treatment. The vas was separated from the cord, ligated and severed with cautery. Pampiniform plexus was ligated, cut and the mass removed en masse. The wound closed in the usual manner. There was no drainage.

Report from Pathologic Department.—The specimen consisted of an irregular lobated mass of tissue from which extended a cord-like structure, 8 cm. long. The main mass was composed of two ovoid structures about the size of walnuts which had been split open. These appeared encapsulated and the cut surface was soft, greyish-white and homogeneous. They were attached closely to an irregularly shaped spongy mass, the cut surface of which had the appearance of testicle.

Sections of the spongy mass showed an outer fibrous capsule within which was atrophic testicular tissue. The seminiferous tubules were small aborted structures widely separated by hyaline fibrous connective tissue, and with large areas of irregular shaped cells between them. These gave the appearance of interstitial cells. In some areas they formed quite large, solid masses.

Sections of the ovoid masses showed them to be lymph nodes, greatly enlarged by the presence of clusters and strings of large immature malignant cells. The normal lymphoid structure was practically destroyed and replaced by these neoplastic cells. They consisted of a large round vesicular nucleus with often four or five large, but not sharply defined, nucleoli and abundant rather granular cytoplasm. In some areas the cells were quite independent with definitely limited cytoplasm, while in other areas the cytoplasm of adjacent cells fused, forming large syncytial masses. Some of the cells lay free in lymphatic channels, and similar cells were present in dilated lymph channels of the testicle. Stained by Laidlaw's method with formalin fixation, the cells were silver positive. The epididymis was free from growth and its tubules contained no spermatozoa.

Anatomic diagnosis was embryonal carcinoma in an undescended testis.

The postoperative course was uneventful. There was some abdominal distention the day following operation but this soon subsided. The spica dressing was changed December 27 and the sutures were removed December 30. The wound was clean at this time and was completely healed January 9, 1934, when the patient was discharged, to return in

a few days for a course of deep x-ray therapy. He is to have several courses periodically.

This case is a most unfortunate one. While in Germany in 1922 the patient lost his right testis following a herniotomy. He then had an orchidectomy for a tumor of the left undescended testis. It is rather tragic that at thirty years of age this patient is sterile and in all probability impotent. He is taking a form of orchitic extract.

Case 2.—J. M., aged forty-eight years, was admitted to the Department of Urology, Royal Victoria Hospital, on January 19, 1934, complaining of: (1) Hematuria, (2) pain in the back, (3) pain in the lower abdomen, (4) sleeplessness, (5) night frequency of urination, and (6) loss of weight and strength.

The patient had measles in childhood and pneumonia at twenty years of age. He had had no other serious illnesses. Family history was essentially negative.

In 1914 the patient noticed a swelling in the right groin. He was able to feel the testicle anterior to the swelling. At no time was the right testicle in the scrotum. The swelling at that time was reducible and gave no trouble until 1918, when severe pain developed. A herniotomy was therefore performed and an attempt was made to bring the testicle down into the scrotum, but without success, so it was anchored in the groin. The patient had no further trouble until March, 1932, when he again began to have a tearing pain in the right groin. A short while afterward he noticed that there was again a swelling in the right groin which was reducible. The swelling gradually increased in size until April, 1933, when it was the size of a small football. At the same time he began to have severe colicky pain in the abdomen. He was admitted to the Hotel Dieu Hospital in Montreal, where on August 29, 1933, a herniotomy was performed and the right testis was removed by Dr. Senecal. This proved to be a mass the size of the head of a newborn babe, and weighed 700 grams. The microscopic examination proved it to be a seminoma. We are greatly indebted to Drs. Senecal and Riopelle for the report of the specimen. The patient made a good recovery and was discharged.

Since this discharge the patient began to have pain across the back, weakness, loss of weight and strength. The pain was most marked over the right loin. In the fall of 1933 he passed bright red blood in his urine on a number of occasions. He had also noticed lately that in spite of a loss of weight his abdomen was getting larger.

On admission the patient seemed fairly well nourished, but was in apparent discomfort for he lay with his knees flexed.

Examination of the head, eyes, throat, neck, chest, and heart showed normal condition and reactions. Blood pressure was 120/85.

There was a mass in the right side of the abdomen just to the right of the umbilicus. It was firm and the size of a man's fist. Liver and spleen were not felt. Flanks were clear.

The nervous system was normal.

There was no costo-lumbar tenderness in the kidneys. No masses were detected in either loin. The kidneys were not palpated. There

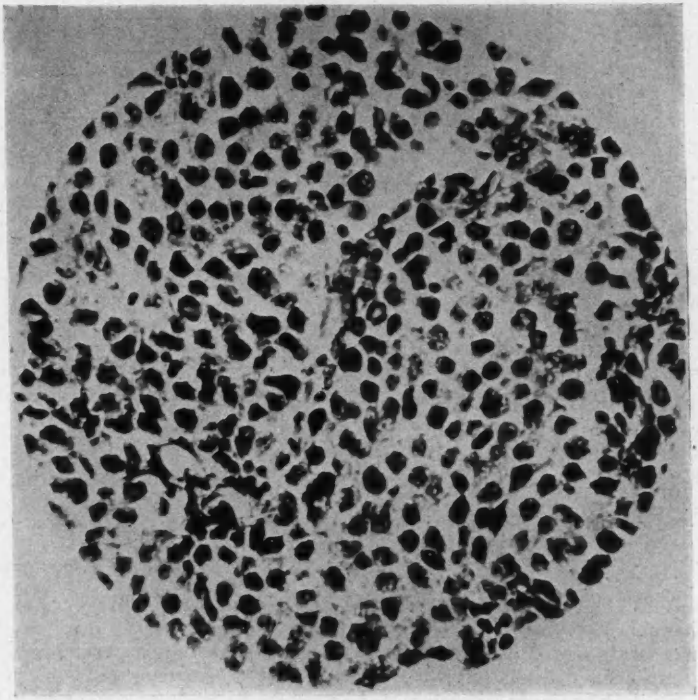


Fig. 2. Case 1. Microphotograph showing large irregular immature cells in a case of an embryonal carcinoma in an undescended testis.

was no tenderness along the course of either ureter. There was slight suprapubic tenderness in the bladder, but no distention. The penis was normal and there was no discharge from the urethra. The left scrotal contents were normal. The right scrotal contents were absent. The prostate per rectum was small, smooth and glandular; no nodules. Seminal vesicles were not enlarged.

Laboratory Data:

Urine: (voided on admission)
Straw clear, 1030, acid (R.B.C. none seen. W.B.C. rare.
Albumin none, sugar none (Epith. present. Bacilli a few.
1 c.c. Phthalein intramuscularly:
First hour, 25 per cent.
Second hour 20 per cent. Total 45 per cent.
Blood Count: Red blood cells.....4,870,000
White blood cells..... 6,000
Hemoglobin.....70 per cent
Blood non-protein nitrogen.....16.80 mgrms. per cent
Blood creatinine ..... 1.15 mgrms. per cent
Van Den Berg—Direct negative.
Van Den Berg—Indirect negative.
Blood Wassermann—negative.
Blood Kahn—negative to *x*.
Blood G.C.F.—negative.

In making cystoscopic examination with a No. F. 24 cystoscope, slight difficulty was encountered through the prostatic urethra. Bladder mucosa was normal. No tumor, foreign body, edema or ulceration was seen. There was no prostatic intrusion. Both ureteral orifices were normal in size, shape and position.

The interureteric ridge was prominent. There was no edema about either orifice and no blood was seen issuing from either. Both ureters were catheterized, the right not so high as the left. Specimen was obtained from the left kidney; only flushing from the right.

Specimens	*Right*	*Left*
Macroscopic	Colorless clear	Straw clear
Volume	3 drops	5 c.c.
Urea:	(not sufficient)	0.007
Microscopic	R.B.C.—None seen.	R.B.C.—Rare.
	W.B.C.—None seen.	W.B.C.—None seen.
	Epith.—None seen.	Epith.—Scattered.
	Organisms—None seen.	Organisms—None seen.

A right pyelogram with 7 c.c. 12 per cent sodium iodide showed no shadow of the iodide in the pelvis and upper ureter. The lower ureter filled and was of normal caliber. At the fourth lumbar vertebra was a cup shaped dilatation with filling defect at superior margin.

Uroselectan series showed good excretion with a well outlined pelvis on the left side, but no excretion of the dye on the right side, even after two hours.

Diagnosis was retroperitoneal metastases from a malignant growth of an undescended testis, right. Metastases in the right kidney(?).

The patient received a course of deep x-ray therapy. He was discharged on February 6, 1934, feeling a great deal better. The mass in the abdomen was just discernible. He is to return periodically for more x-ray treatments.

In this instance we are undoubtedly dealing with a case of

metastases of the retroperitoneal glands secondary to a malignant growth of an undescended testis. The fact that we have been unable to outline the right renal pelvis either by retrograde or intravenous pyelography suggests the presence of metastases to the right kidney as well. A history of hematuria strongly points to that decision. A rather interesting point in this case is the very large size of the inguinal growth. Seven hundred grams is quite a size and is equivalent to more than 1.5 pounds.

SUMMARY AND CONCLUSIONS

1. Two cases of malignant disease in undescended testes are here reported.

2. A brief review of the literature is given.

3. There are no substantial facts to prove that undescended testes are predisposed to malignant change.

4. The pathology and treatment of malignant disease of undescended testes are the same as those of normally placed organs.

5. No case of cryptorchidism *per se* should be subjected to orchidectomy.

REFERENCES

1. ADAMI, J. G.: Principles of Pathology. Vol. 2, 1909.
2. COLEY, W. B.: Cancer of the testis. Ann. Surg., 62:40, 1915.
3. CUNNINGHAM, J. H.: New growths developing in undescended testicles. Jour. Urol., 5:471, 1921.
4. ECCLES, W. M.: Quoted by Hinman.
5. HINMAN, FRANK: Modern Urology (Cabot), 1:580, 1924.
6. KOCHER: Quoted by Hinman.
7. LUND, F. B.: New growths in undescended testicles. Boston Med. and Surg. Jour., 190:533, 1924.
8. MACKENZIE, D. W., and RATNER, MAX: Tumors of the testis. A brief series with special reference to the pathology and clinical malignancy. Surg., Gynec. and Obstet., 52:336, (Feb. 15) 1931.
9. MARSHALL: Quoted by Rea.
10. REA, C. E.: Malignancy of the testis with special reference to undescended testis. Report of seventy-six cases. (Seventeen cases previously reported.) Amer. Jour. Cancer, 15:2646, 1931.
11. VASTOLA, A. P.: Embryonal carcinoma of abdominal testis in a pseudohermaphrodite. Jour. Am. Med. Assn., 101:111, 1933.
12. TAYLOR, G.: The aberrant testicle—a plea for castration. Clin. Jour. Lond., 47:26, 1918.

NUPERCAIN AS A SPINAL ANESTHETIC

WITH SPECIAL REFERENCE TO THE EMPLOYMENT OF NUPERCAIN SOLUTION OF HIGH DILUTION

HOWARD S. JECK, M.D.

From the Urological Services of Bellevue and the New York Hospital (Cornell Division), New York City

Spinal anesthesia has steadily increased in popularity during the past ten years. For several decades, urologists have recognized its advantages, chief among which are its relatively harmless effect on the kidneys and the unusual degree of relaxation it affords. Because of the latter property, spinal anesthesia is now widely used as well by general surgeons, gynecologists and obstetricians.

The chief problem has been to find a spinal anesthetic which is safe and lasting and at the same time productive of a minimum of troublesome sequelæ.

Nupercain introduced abroad as *percain*† seems to have fulfilled these requirements to a remarkable degree. Keyes and McLellan, in an article published in 1930, were among the first in this country to direct attention to its virtues.

Until approximately eighteen months ago the preparation of nupercain used almost exclusively in America as a spinal anesthetic was the 1-200 solution which is usually given in the following manner: The spinal canal is usually tapped either between the first and second, or second and third lumbar vertebræ. When the spinal fluid appears, a 10 c.c. syringe containing the nupercain solution (2 c.c.) is attached to the needle. Spinal fluid is allowed to collect in the syringe to the amount of 5 to 10 c.c. The mixture of nupercain and spinal fluid is then slowly injected into the spinal canal. Barbotage is employed to make the preparation reach certain levels. Some prefer to inject the nupercain at higher levels for the higher operations rather than depend on barbotage. But this method of employing nupercain has proven to be rather capricious, especially in operations requiring anesthesia at the higher levels. While many perfect anesthesias are obtained, there are likewise too many

†A quinolin derivative, percain is known chemically as a-butyl-oxycinchononic acid diethyl ethyl-endiamide hydrochloride.

incomplete anesthesias, even in the hands of the expert, to commend it as an ideal spinal anesthetic.

On the Bellevue Urological Service spinal anesthesia has been almost exclusively employed for the past fifteen years. Novocain, in some form or other (crystals or "spinocain") was the drug of choice until about four years ago, when we began to use the concentrated nupercain solution particularly in the operations requiring anesthesia at a high level (kidney and high ureteral operations). Only about two-thirds of these operations could be finished without supplementary anesthesia of some sort, while in many operations there was no analgesia from the spinal anesthetic at all. But the value of nupercain was so well appreciated, chiefly on account of its lasting effect, that we were loath to give it up. New batches of nupercain were employed and the technic of injecting it was rigidly investigated, particularly in regard to having the syringes and needles alkali-free. Despite these precautions, concentrated nupercain remained an uncertain preparation. The opportunity, therefore, to try out another preparation of nupercain which had been very successfully used abroad, was very welcome. This preparation differs chiefly from the 1-200 solution by its greater dilution (1-1500) and the fact that the diluent is a 0.5 per cent saline solution. It is therefore hypobaric: its specific gravity is less than that of spinal fluid. Employed first by the English anesthetist, Mr. Howard Jones, the preparation is known also as "Jones' solution."§

Hewer explains the advantages of Jones' solution as follows:

"The subarachnoid space is treated in exactly the same way as other tissues in an infiltration analgesia, in that a relatively forcible injection of a large volume of a dilute solution is made; no fluid is withdrawn, and the level of analgesia is determined entirely by the amount of fluid injected. This is obviously more accurate than the older method of injecting a small volume of a concentrated solution of stovain or novocain, since, even if such a solution be artificially 'lightened,' the heavier constituents will become subject to gravitational diffusion when

§The concentrated (1-200) nupercain solution is put up in 2 c.c. ampules, each ampule containing 10 mgm. of nupercain. The usual amount required for one spinal anesthesia is 2 c.c. Jones' solution of nupercain (1-1500) is put up in 20 c.c. ampules, each ampule containing approximately 13.3 mgm. Rarely ever is it necessary to give more than 15 c.c. of the 1-1500 solution of nupercain for any type of operation and the majority of high operations require only 12 or 13 c.c. of the solution. Therefore, the usual dose of the concentrated (1 to 200) nupercain solution is equivalent to the usual maximum dose of the dilute (1-1500) solution and the majority of high operations may be performed after only 12 or 13 c.c. of the dilute solution are given. Since alarming results in spinal anesthesia are often due to unnecessarily large doses of the preparation, one keeps well within the maximum dose of nupercain when 13 c.c. (approximately 8.5 mgm.) of Jones' solution are employed.

admixture with cerebrospinal fluid takes place, and the result must be uncertain."

The technic employed in giving the dilute solution of nupercain, "Jones' solution," is as follows:

The patient is placed on his side in the usual position for a spinal tap. (It should not be injected with the patient sitting up because of its low specific gravity and its tendency, therefore, to rise high in the spinal column.) For all operations, high as well as low, the preparation is injected low, that is usually between the first and second lumbar veretbræ. The spinal tap is made in the usual manner and, without withdrawing any spinal fluid, the solution is slowly injected, the amount depending on the height the anesthesia is supposed to reach and to some extent on the duration of the operation. For kidney operations usually 12 to 15 c.c. of solution are required. For bladder operations, unless prolonged, scrotal operations and perineal operations, it is rarely necessary to give over 10 c.c. For the reason that the solution is hypobaric, the patient should lie on the side opposite to that of the organ to be operated upon; for example, a patient on whom it is proposed to perform a right nephrectomy should lie on his left side. After the injection is made the patient is turned on his face and the head of the table is slightly depressed with the foot elevated, in which position he is allowed to remain for five minutes. He is then placed in the position required by the operation, which may start at once.

At Bellevue, "Jones' solution" was used first only in kidney operations. The improvement in the number of successful spinal anesthesias and the duration of the anesthetic became at once apparent. Later "Jones' solution" was used in suprapubic cystotomies, prostatectomies, external urethrotomies, and other low operations with even greater success. We then began to employ "Jones' solution" in the New York Hospital Urological Service, recently opened, where the concentrated nupercain solution and novocain were the preferred drugs for spinal anesthesia.

In order to obtain some idea of the relative value of the Jones' solution or solution of high dilution, as compared with the concentrated dilution, the results of 171‡ anesthesias given on the Bellevue and New York Hospital Urological Services, Cornell Division, have been analyzed. These have been divided into high operations, including all kidney operations and operations on the upper

‡These figures by no means represent the total number of nupercain spinal anesthesias given in the two services. Data were taken only from the charts which contained the most complete records pertaining to the anesthesia and its after-effects.

third of the ureter, and low operations, or all operations below the junction of the upper and middle thirds of the ureter. The latter group includes all types of low ureteral, bladder, scrotal, and perineal operations. In both the high and low groups, both the concentrated and dilute solutions of nupercain were used.

In our series of patients the chief advantage of the 1-1500 solution of nupercain over the 1-200 solution in high operations is shown in Table I. Successful anesthesias induced by the dilute

TABLE I

*High Operations**

	No. of Anesthesias	Satisfactory Anesthesias	Supplemented by General Anesthesia
Concentrated Nupercain 1-200 sol.	47	32 (68%)	15 (32%)
Dilute Nupercain 1-1500	61	55 (90%)	6 (10%)

Low Operations

	No. of Anesthesias	Satisfactory Anesthesia	Supplemented by General Anesthesia
Concentrated Nupercain 1-200 sol.	36	34 (94.5%)	2 (5.5%)
Dilute Nupercain 1-1500	27	26 (96%)	1 (4%)

solution 90 per cent; successful anesthesias induced by the concentrated solution 68 per cent. Even in the group of low operations where almost any spinal anesthetic gives reasonably satisfactory results, the percentage of successful anesthesias from the dilute solution is slightly higher than that of the concentrated group.

*In the high operations where the concentrated nupercain solution was employed, there were 24 nephrectomies, 14 pyelotomies and nephrotomies for stone, and 9 other kidney and high ureteral operations.

In the high operations where the dilute nupercain solution was employed, there were 31 nephrectomies, 22 pyelotomies and nephrotomies for stone, and 8 other kidney and high ureteral operations.

Troublesome Sequelæ.—In Table II, vomiting, headache, and distention as troublesome sequelæ following the use of both the concentrated and dilute solutions of nupercain are considered. The figures are presented with some reservation particularly with reference to vomiting and distention for it is fully realized that both of these conditions may be influenced by other factors.

In the high operations especially, *distention* due to the anesthetic itself should not be taken too seriously. As is well known a sur-

TABLE II

High Operations

	Number Analyzed	Vomiting	Headache	Distention
Conc. Nupercain (1-200 sol.)	22	8 (32%)	3 (14%)	9 (41%)
Dilute Nupercain (1-1500 sol.)	60	23 (38%)	8 (13%)	28 (46.6%)

Low Operations

	Number Analyzed	Vomiting	Headache	Distention
Conc. Nupercain (1-200 sol.)	32	13 (4%)	2 (6%)	6 (2%)
Dilute Nupercain (1-1500 sol.)	24	7 (3%)	1 (4%)	10 (42%)

prisingly large number of operations requiring manipulation of the kidney and pulling on the kidney pedicle, performed under any type of anesthesia except spinal, are followed by a considerable degree of distention. However, in most instances the distention following nupercain, either concentrated or dilute, is fairly transient and does not present a serious problem. In the high operation group, distention following the dilute nupercain solution is somewhat more marked than that following the employment of the concentrated solution, while in the low operation group the difference in favor of the concentrated solution is considerable.

Evidently *vomiting* depends a great deal on the level to which the anesthetic extends. This is rather well borne out by the fact that in the high operations vomiting occurred in one-third or more of the patients where either the concentrated or dilute nupercain solution was given, the latter causing a slightly higher percentage

of cases of vomiting than the former. This discrepancy between the two solutions may be explained by the possibility that the dilute nupercain reaches a higher level in most instances than the concentrated. Compare these figures with the low operation group where the percentage of vomiting caused by both dilutions is very low and almost equal. Vomiting, however, is never a very troublesome factor, and usually disappears with the disappearance of analgesia.

Headache, one of the most troublesome of spinal anesthesia sequelæ, is apparently encountered no oftener in nupercain-induced spinal anesthesia than the headache of spinal anesthesia from other anesthetics. Here, as in the case of distention and vomiting, the percentage was higher in the high operations than in the low operations. The difference between the headaches following the use of the concentrated solution, and those following the use of the dilute solution is slight, and in favor of the dilute solution as shown in the table.

TABLE III

Patients	Operation	Amount of Nupercain 1-1500 sol.	Time of Operation	Comments on Anesthesia
1.	Pyelotomy for stone	15 c.c.	50 min.	Satisfactory for 45 min. During last 5 min. pain in region of incision.
2.	Nephrectomy for tumor and hydronephrosis	15 c.c.	1½ hrs.	Satisfactory until suture of skin
3.	Nephrectomy for tuberculosis	13 c.c.	1 hr.	Satisfactory until fat was pulled from upper pole of kidney.
4.	Nephrectomy for carcinoma of kidney	13(?) c.c.	85 min.	Satisfactory until pull was made on kidney pedicle; then general anesthesia.
5.	Nephrectomy for tuberculosis	15 c.c.	70 min.	Satisfactory until pull was made on kidney pedicle. Gas and oxygen after kidney was excised.
6.	Nephrectomy for stone	15 c.c.	50 min.	Good relaxation, but patient seemed to have pain.

Table III, pertaining to the six failures in the group of high operations where the dilute nupercain solution was given, shows in

each case the amount of anesthetic employed, the time consumed by the operation, and a brief description of the extent of the anesthesia produced. It can be readily seen here that in no instance, except the last one, was the anesthetic a complete failure.

The unsatisfactory anesthesias in Table III are fairly representative of the high operation concentrated nupercain group as well, except that in this group there were several instances where there was no analgesia at all. In these cases, it is quite probable that the anesthetic was not injected wholly within the spinal canal, despite the careful technic and appearances to the contrary.

Behavior of the Blood Pressure.—While blood pressure readings were taken during all the operations they are not particularly stressed, due largely to the fact that the blood pressure is more or less influenced by the initial dose of ephedrin which is given to nearly all patients immediately before the spinal anesthetic is injected, the exceptions being an abnormally high blood pressure at the outset. As a rule blood pressures behave in one of the three following manners:

1. The systolic pressure may immediately rise twenty or thirty points (ephedrin effect), then drop fifteen or twenty points and proceed more or less at a normal level throughout the balance of the operation.

2. The blood pressure may drop rapidly in the beginning (thirty to fifty points during the first twenty minutes of the operation) and then on the second injection of ephedrin rise to its former level and proceed more or less at this level through the operation.

3. In the third group the blood pressure is hardly influenced at all and proceeds along at the same level throughout the operation.

In all three groups the diastolic pressure does not drop as readily or relatively as far as the systolic pressure, while the pulse rate in many instances apparently is not affected until a few minutes after the systolic pressure changes. In general the fall in blood pressure is somewhat more rapid with the dilute nupercain solution, especially in the high operations, than is the case with the concentrated solution. However, the difference is too slight to be a factor in a choice between the two solutions.

But too much importance should not be ascribed to blood pressures. I agree with Hewer, who believes it is a mistake to take

frequent blood pressure readings, for it disturbs the patient. As a rule, satisfactory information of the patient's condition can be obtained by watching the patient's color and if the anesthetist is then in doubt the blood pressure should be taken.

With both the dilute and concentrated nupercain solutions the respirations are usually shallow and regular, but respiratory failure is, of course, an ever present danger. Should it occur, a mixture of carbon dioxide and oxygen should be forced into the patient's lungs by means of an inhalation apparatus, for as Hewer has pointed out, "respiratory failure is less likely to occur from phrenic paralysis than from fatigue of the respiratory center, caused by the anoxemia resulting from imperfect lung ventilation, which, in turn, is due to temporary paralysis of most of the intercostal muscles. The carbon dioxide and oxygen should rapidly restore regular breathing unless the center has already been narcotized by the large doses of morphine, avertin or similar drugs."

In connection with the advantages of one solution of nupercain over the other the question arises, "why not employ the concentrated nupercain solution, diluting it up to 14 c.c. or more, with spinal fluid, and then proceed as one does with the dilute solution, thereby avoiding a large amount of a foreign solution in the spinal canal?" The objections to this method are: (1) a hypobaric solution of nupercain is not obtained in this way, and (2) in many instances it is difficult to withdraw enough spinal fluid (especially with the patient lying on his side) to afford the proper dilution.

I am indebted to Dr. I. D. Makowski of the Bellevue Urological House Staff for his help in obtaining the necessary data from the patients' charts. My thanks are also due the Ciba Company of New York for their generosity in supplying the nupercain solutions, and for their coöperation in other ways.

RÉSUMÉ

1. While the dilute solution of nupercain may produce a slightly greater percentage of the unfavorable sequelæ than the concentrated solution, such as abdominal distention and headache, it is, generally speaking, a far more satisfactory anesthetic than the concentrated solution because of the much higher percentage of cases wherein satisfactory analgesia is produced.

2. Approximately four-fifths of the maximum dose of the dilute nupercain frequently gives as great a degree of anesthesia as is obtained from the entire dose of the concentrated solution.

REFERENCES

1. HEWER, C. L.: High spinal block analgesia with percain. Anesthesia and Analgesia, 11:29-32, (Jan. and Feb.) 1932.
2. KEYES, E. L., and MCLELLAN, A. M.: Preliminary report on a new local anesthetic (nupercain), Am. Jour. Surgery, 9:1-8, (July) 1930.

THE TREATMENT OF MALIGNANT DISEASE OF THE PENIS

ROGER C. GRAVES, M.D.

From the Urological Clinic of the Pondville Hospital (Massachusetts Department of Public Health), Boston, Massachusetts

Carcinoma of the penis represents, according to Ewing, from 1 to 3 per cent of all cancers in male patients. Certainly the disease is not commonly encountered in clinical practice. In 20,400 case histories at the Brady Urological Institute, Lewis reports that there were 2,017 cases of malignant disease, including seventy cases of epithelioma of the penis, an incidence in the tumor group of 3.5 per cent. Leighton, writing from the Barnard Free Skin and Cancer Hospital in St. Louis, has presented another excellent recent discussion of the subject, and has reviewed a series of sixty-seven cases seen during a period of twenty-eight years. My own particular interest has been aroused by the fact that, in spite of its relative rarity, twenty-eight cases of cancer of the penis have happened to come under my personal observation within the past seven years. I wish to discuss solely the treatment of the disease, and to suggest a modified operative technic for those patients for whom the commonly advocated drastic procedure involves unwise or unnecessary risks.

In the consideration of therapy, it is important first to bear in mind that the usual carcinoma of the penis is not a radio-sensitive tumor and that it is not safe, therefore, in most instances, to place reliance for cure upon radium and x-ray alone. I believe that only the smallest, most superficial lesions should be regarded as suitable for treatment exclusively by these agents. We must not forget, moreover, that even in such early cases the groins require just as close scrutiny and may need just as vigorous therapy as in the more advanced conditions. Where there is deeper, more extensive involvement, invading the substance of the organ rather than its integument, and when, as is so often the case, there is associated infection, the best hope of successfully eradicating the disease lies in direct surgical methods.

Concerning the choice of operation, it has been my feeling that

a partial amputation may be performed when it is possible to remove the growth and still leave sufficient stump to give the patient a good trajectory for urination in the standing position. Otherwise, as compared with a retracted dimple in the scrotal skin, complete amputation and a well-constructed perineal urethra will afford greater comfort and better hygiene. Regardless of this consideration we are led sometimes to advise the simpler procedure for those

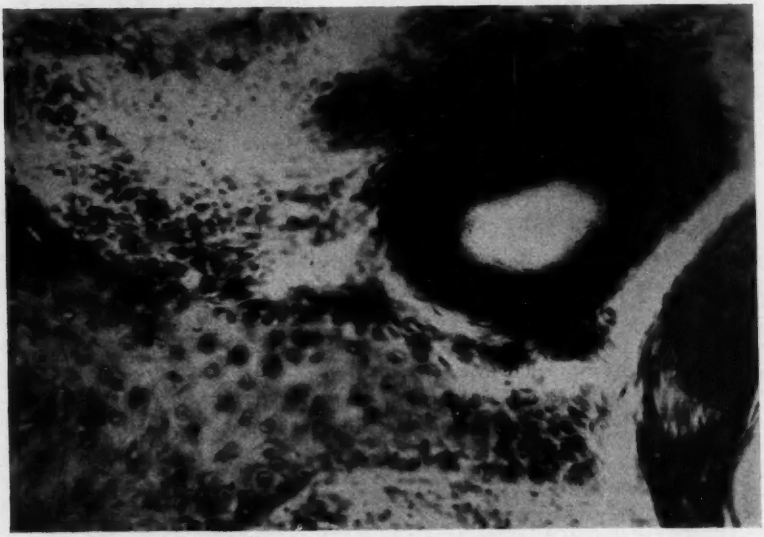


Fig. 1. Photomicrograph of epidermoid carcinoma of the penis, grade 1. One large epithelial pearl and a portion of another one are shown together with heavily keratinized, well differentiated epithelial cells clearly demarcated from their stroma (Shields Warren).

who are in poor condition, but I am not sure, even in such cases, that the complete removal involves as much as we fear of added risk, provided, of course, that the gland dissection is postponed until another day (Fig. 11).

The classical operation for cancer of the penis, as commonly described, includes a sweeping incision across the lower abdomen for the excision of inguinal and femoral lymph nodes; and communicating with an incision around the organ for its partial or

complete amputation. Thus all structures are removed *en bloc*. The scrotum is sometimes bisected, in approaching the perineal urethra, and occasionally even the scrotal contents have been removed with the rest of the mass. All this represents a formidable undertaking and for many cases I believe it to be excessive. Often these patients have passed well beyond middle life and their general physical reserve has been undermined by age, urinary obstruction, sepsis, and

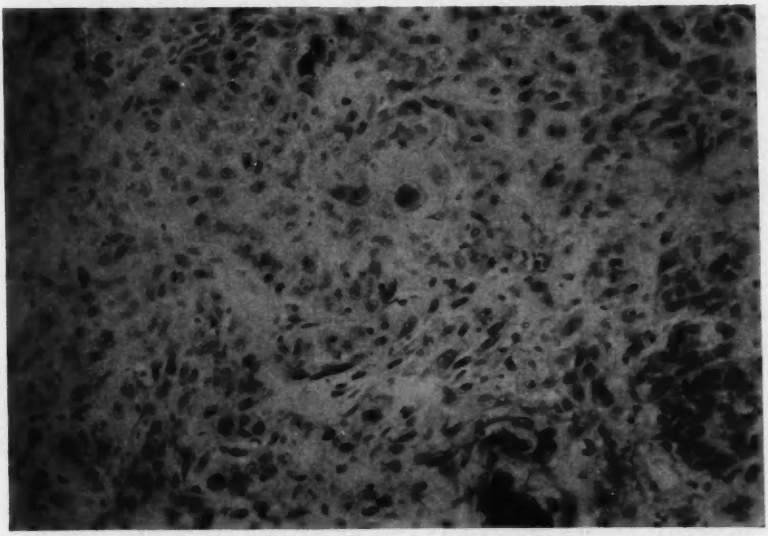


Fig. 2. Photomicrograph of epithelial carcinoma of the penis, grade 2. On one side of the section an attempt at pearl formation is shown. Some cells are keratinized, but more are unkeratinized. Several mitotic figures are present. There is no clear-cut demarcation between the tumor and the stroma (Shields Warren).

the presence of malignant disease. For them, the drastic operation that is generally advised involves grave risks as to life and almost certainly, where there is recovery, delayed healing and a long, difficult convalescence. In Young's series, the average number of postoperative days was forty-four. Such widely dissected skin flaps in such patients may be expected to heal badly and they frequently do, with resulting serious toxemia from so extensive an area of slough and secondary infection. The scrotum, which is heavy with vascu-

lar stasis and lymphedema under these circumstances, often plays an important part in the breaking down of the wound, by its pull against the weakening lines of suture.

To be sure, we have been taught to assume these risks for the sake of removing the intervening lymphatic channels at the same time and together with the primary growth and its regional nodes. This is done with the breast where it is relatively easy and safe; it is not considered routinely in the tumors of the head and face, which really offer a closer analogy, histologically, to the neoplasm under discussion. There is undoubted advantage, at least in theory, in the radical operation for cancer of the penis in favorable cases, but I submit that this advantage will not outweigh, in the more hazardous cases, the clinical benefits of lowered mortality and quicker recovery from a less radical program. The chance of disseminating this type of tumor at the point of division of an intervening lymphatic between the penis and the groin, is exceedingly slight. I am informed that usually the Grade 2, 3, and 4 cases metastasize embolically along lymph channels, while only Grade 1, which grows but slowly, advances by direct permeation, if at all, along these paths. It is my feeling that, except perhaps in the younger, well-nourished individuals, the end-results will be as good and the immediate results better, if a modified incision such as I will describe is employed and if, in many instances, the gland dissection is done later, rather than at the time of the amputation. Certainly when the groins are already invaded there can be no argument, and in the average case without metastasis, I doubt that the dangers will be appreciably greater. In this as in all our problems, however, nothing is proved except by the rigid controls of time and repeated experience.

Concerning operative technic, it can be said that the partial amputation of the penis may be carried out by any standard method, but the line of incision should be at least 2 cm. proximal to any palpable thickening in the region of the growth. The stump of the urethra should always be left a little longer than the stump of the corpora, and the actual division of the latter is done best with high frequency current. Coagulation controls hemorrhage and lessens the likelihood of the dissemination of tumor cells.

The complete removal of the penis is said to have been suggested first by Thiersch of Leipzig in 1875. An historical survey of the

literature since that time has been published by Leighton in his recent excellent paper. There are minor variations in detail as one reads the reports, and some differences of opinion. Cunningham, for example, has employed the drastic extirpation of penis and glands through one incision which also divides the scrotum for the construction of a perineal urethra. Young, on the other hand, recommends the same sweeping inguinal dissection, but prefers to leave the urethral stump in its normal position. Good results will be obtained with any method which removes all the disease, without subjecting the patient to unreasonable and unnecessary risks.

The simplified technic which I am using in advanced and hazardous cases and which seems at least worthy of trial, is as follows:

There should be first a period of supportive medical care varying in duration and character with the needs of the individual case. This is of the greatest importance and careful attention should be directed to reducing the activity of local infection as well as to the general upbuilding of the patient. For anesthesia spinal novocain is usually employed. Unless the groins are to be dissected, the patient is placed at once in lithotomy position. The alcohol-acetone solution of mercurochrome is satisfactory for the preparation of the skin, since it does not give the scrotal irritation which sometimes follows iodine. The portion of the penis involved in tumor is covered with sterile rubber dam or alcohol gauze. No instrument is placed in the urethra. This is not necessary, and it is unwise in the presence of growth around the meatus.

A vertical, midline suprapubic incision is made, extending upwards far enough so that the scrotum will be drawn well away from the perineum when its upper portion is attached to the apex of this wound at the close of the operation. The lower pole of the incision reaches the base of the penis where it encircles the organ and penetrates as far as the actual fibrous sheaths of the corpora cavernosa and spongiosum. This can be done very quickly and it is not necessary to bisect the scrotal wall. The fat overlying the symphysis and the rectus fascia and lying between the medial aspects of the spermatic cords at the base of the penis is dissected away for removal with the penis itself (Fig. 3). The corpus spongiosum is now cut across with the high frequency knife well proximal to the tumor and at a level which will allow sufficient length of urethral stump for transplantation without tension into the peri-

Fig. 3.

Fig. 4.

Fig. 3. Artist's drawing. Operation for complete amputation of the penis. The vertical midline suprapubic incision is shown, and the incision encircling the base of the organ. This permits sufficient traction to readily expose the spermatic cords. The fat over the symphysis is being dissected away for removal with the penis itself.

Fig. 4. Artist's drawing. Operation for complete amputation of the penis. The corpus spongiosum is being dissected away from the corpora cavernosa.

neum. A soft bougie then passed into the opened urethra aids in dissecting the spongiosum away from the corpora (Fig. 4). Great care must be used to avoid urethral injury, for there is no ready line of cleavage until one approaches the region of the bulb where the separation becomes relatively easy. The corpus spongiosum must be freed until it can be brought straight through a small stab wound in the perineum, between scrotum and anus, without the least angulation or tension. Fingers worked downwards from above, back of the scrotum, readily prepare the way for this perineal opening (Fig. 5). Midline splitting of the scrotal wall will be found unnecessary and serves only needlessly to complicate the wound. The removal of the testicles, of course, is wholly without justification, in most cases.

Moist gauze and a wooden spatula are placed between the roots of the cavernous bodies and the bulb to prevent injury of the urethra when the corpora are finally amputated near their attachments, with a mildly coagulating current. The open ends of the stumps are closed over, either separately or together, with a continuous lock suture of chromic catgut. It will help also in hemostasis if a transfixing suture is placed around the region of the suspensory ligament and dorsal arteries when the base of the penis is first freed at the start of the dissection. There is no point in meticulously removing all of the root of each corpus down to the point of its actual union with the ischiopubic ramus.

The urethral stump should protrude at least 1 cm. beyond the skin of the perineum at the end of the operation, any redundant portion being cut away. It is not slit, for with care in the avoidance of trauma, there need be no contracture of the new meatus. Subcuticular mattress stitches of fine chromic catgut are used to anchor the stump in position, one on each side and one posteriorly. A wick of rubber tissue emerges in front of the urethra anteriorly, at the close of the operation. This leads from the region of the base of the penis and provides downward drainage through the space back of the scrotum.

A wick of iodoform gauze is left in one angle of the upper wound for temporary drainage and the cut edge of the scrotum in the midline is approximated to the apex of the suprapubic incision (Fig. 6). The final skin stitches should be supported by a row of deeper sutures in the fat layer. Lastly, a small, soft rubber catheter is

Fig. 5.

Fig. 6.

Fig. 5. Artist's drawing. Operation for complete amputation of the penis. The region back of the scrotum is readily entered with the fingers in preparation for the stab wound in the perineum, through which the urethra is drawn. It is not necessary to bisect the scrotum.

Fig. 6. Artist's drawing. Operation for complete amputation of the penis. The cut edge of the scrotum in the midline has been approximated to the apex of the suprapubic incision, thus drawing the scrotum well away from the new urinary meatus.

usually passed to the bladder and lightly secured to the urethra by a stitch of very fine silk or catgut for the first few days, but this is probably not strictly necessary as comfortable urination with good control may be expected from the start. Certainly the catheter,

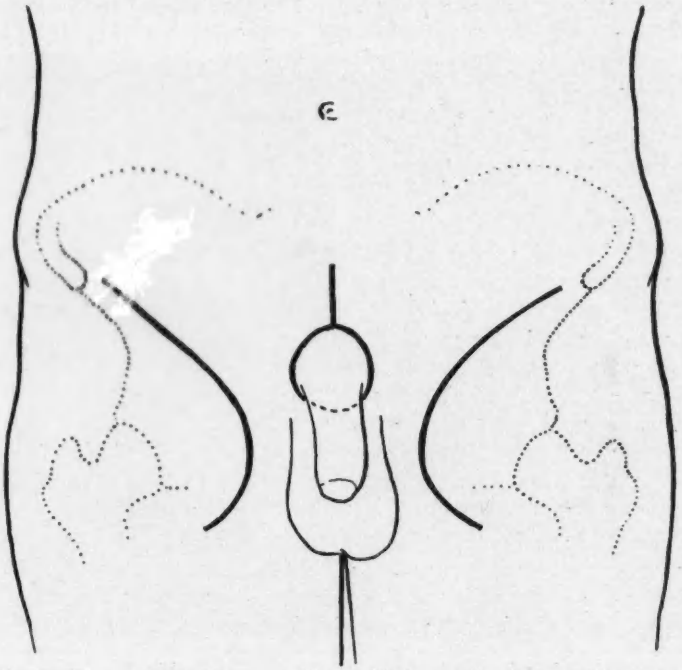


Fig. 7. Diagram of incisions used in modified operation for complete amputation of the penis and dissection of the superficial gland-bearing areas. Note the curved incisions in the groins. As the wounds are not continuous across the midline, better healing may be expected.

if used, should be removed just as soon as one can count upon the full coöperation of the patient.

An important part of the after-care lies in the dressings. There should be always a roll or pad in the perineum in front of the urethra and held firmly in place by a perineal binder. This obliterates the newly opened space in the region back of the scrotum, and by

elevating the scrotal wall serves also to protect the suprapubic suture line from undue tension.

Whether the inguinal regions are dissected at the time of the amputation of the penis, or at a second operation some time later, the dissection is carried out through an incision which is shown in the accompanying diagram (Fig. 7). It begins medial to the anterior

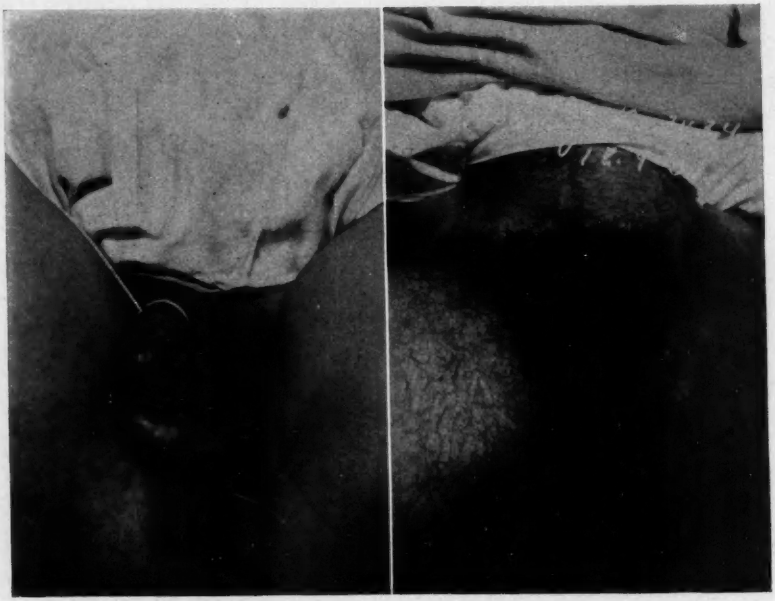


Fig. 8. Fig. 9.

Fig. 8. Photograph of epidermoid carcinoma of the penis, grade 2. Pondville Hospital case 3434. The patient was an Italian laborer, aged forty-one. Complete amputation and bilateral groin dissection were performed on July 1, 1931. Inguinal metastases were not found. The patient was last seen in good condition April 1, 1934 (See Figs. 9 and 10).

Fig. 9. Photograph of patient after operation (See Fig. 8).

superior spine and extends parallel with Poupart's ligament and a little above it, to within about one finger's breadth of the spine of the pubis where it curves downwards and outwards across the area of the femoral triangle. This affords a much more adequate exposure than a simple oblique incision in the groin, and it avoids the

poorly healing corners of a T-shaped wound. All palpable nodes and the gland-bearing fat are removed *en masse* as far medially as the spermatic cord and the external ring. Young calls attention to a lymph channel lying under the spermatic cord and a small node which may be found at the external inguinal ring. The dissection must be carried well downwards over the thigh also, for in my experience a gland is often found much farther distally than one ex-

Fig. 10.

Fig. 11.

Fig. 10. Photograph showing perineal urethra (See Figs. 8 and 9).

Fig. 11. Photograph of advanced epidermoid carcinoma of the penis, grade 3. Pondville Hospital case 7754. There were markedly enlarged inguinal lymph nodes. The patient was eighty-three years of age and was in poor condition for extensive surgery, but removal of the tumor seemed imperative as it was a swollen, infected, malodorous mass. Complete amputation of the penis was performed using the method herein described on May 9, 1934. Sacral anesthesia and 2 per cent novocain locally were found to be sufficient, and the added risk of general or spinal anesthesia was avoided. The groins were not dissected, but there was a marked and prompt diminution in the size of the inguinal nodes following operation. The patient made a satisfactory recovery and left the hospital on June 9, 1934. It seems quite certain that he would not have withstood a more radical procedure.

pects, along the saphenous vein. A segment of this vein will be included usually in the mass removed. Especial care must be used, of course, to dissect the inner aspect of the femoral vein and the region leading into the crural canal. Thus far, I have not continued the dissection beneath Poupart's ligament to include the iliac nodes in the structures removed.*

High voltage x-ray therapy directed to the femoral, inguinal, and deep pelvic regions should be used in all cases following surgical dissection and in those cases in which, for one reason or another, such dissection has not been undertaken. We still lack the basis for agreement concerning the value of x-ray treatment of the groins as a pre-operative measure. In theory, it should be useful if lymphatic and vascular channels may be closed in this way, and so lessen the danger of the further dissemination of disease at the time of operation. If so, what should be the interval between the two procedures? It is our purpose to study histologically sections removed from the superficial gland-bearing areas at various intervals after deep therapy in an effort to throw further light upon this problem. I feel quite sure, however, purely from the standpoint of clinical experience, that a satisfactory dissection of the groins after x-ray treatment has been given, must be done not too early, in the stage of acute congestion and edema, and not too late when fibrosis has occurred. It is our present opinion that six to eight weeks may prove to be a satisfactory interval.

REFERENCES

BARRINGER, B. S., and DEAN, A. L.: Epithelioma of the penis. Jour. Urol., 11:497-514, 1934.

CUNNINGHAM, JOHN H.: The operative treatment of carcinoma of the penis. Surg., Gynec. and Obstet., 19:693-699, 1914.

EWING, JAMES: Neoplastic Diseases. Philadelphia and London: W. B. Saunders Co., 844, 1919.

KAUFMANN, C.: Verletzungen und Krankheiten der männlichen Harnröhre und des Penis. Deutsche Chirurgie, Stuttgart, 50A:295, 1886.

LEIGHTON, W. E.: Carcinoma of the penis, with a report of sixty-seven cases. Amer. Jour. Cancer, 16:251-276, 1932.

*I find, in reviewing the literature, that Sir William MacCormac, who reported five cases of amputation of the penis for epithelioma, in the *British Medical Journal* of February 20, 1886, described a "buttonhole" wound in the perineum, through which he brought the urethra without bisecting the scrotum, and also a separate "curved incision" for the removal of a glandular mass in the groin. Puzey, in 1884, also made use of a stab wound in the perineum for the transplantation of the urethra. Kaufmann agreed with Demarquay that there is advantage in a second-stage gland dissection.

LEWIS, LLOYD G.: Young's radical operation for the cure of cancer of the penis. Jour. Urol., 26:295-316, 1931.

MACCORMAC, SIR WILLIAM: Five cases of amputation of the penis for epithelioma. Brit. Med. Jour., 343-345, (February 20) 1886.

PUZEY, CHAUNCY: Epithelioma of penis; complete amputation with formation of perineal urethra. Lancet, 2:912-913, 1884.

YOUNG, HUGH H.: Practice of Urology. W. B. Saunders Co., Philadelphia and London, 1927.

YOUNG, HUGH H.: A radical operation for the cure of cancer of the penis. Jour. Urol., 26:285-294, 1931.

DISCUSSION

DR. NATHANIEL P. RATHBUN (Brooklyn, N. Y.): With regard to spinal anesthesia, I think for the ordinary case, requiring an hour or less in time, novocain in doses of 100 milligrams has been pretty uniformly successful in my hands. In the cases which I anticipate are going to take a longer period of time, I have been using a mixture, from 100 to 120 milligrams of novocain, depending on the size and weight of the individual, to which is added 5 milligrams of nupercain. This gives at least an extra hour of anesthesia and in my hands has been very satisfactory.

DR. VINCENT J. O'CONOR (Chicago, Ill.): I would like to ask the members of this Association whether in their experience they have ever seen an instance of metastases of carcinoma from either the foreskin or glans penis which has completely skipped the regional inguinal lymph nodes and metastasized to the spine or some adjacent structure? From my own experience, from what I have been able to read, and from the nature of the lymphatic drainage in this region I have always felt that the superficial or deep inguinal nodes were involved wherever metastases occurred from a cutaneous lesion in this region.

This belief was recently discredited when a patient, who had had a simple local resection of a malignant tumor of the foreskin elsewhere, developed metastases in the lumbar vertebræ, the sections of which were identical with the sections of the original tumor removed from the penis and yet there were absolutely no palpable superficial or deep inguinal lymph nodes on either side.

This patient was brought to the hospital to have his tonsils removed, thinking that they might be providing a focal infection for the backache of which he had complained for a period of two years. The backache had been present for eighteen months before he noted the small nodule on the foreskin. This latter had been removed only six weeks before entrance to our hospital. Following his tonsillectomy he was unable to void and had to be catheterized continuously from that time on.

A week later I saw him in consultation and made a diagnosis

of a spinal bladder, the subsequent cystoscopic findings, et cetera, being typical of this condition. Following this diagnosis three well known neurologists examined this man and found no evidence of anything that would indicate any spinal disease. Excellent x-ray studies of the spine had been made on several occasions prior to my seeing him and a set made at this time showed no evidence of any disease except possibly a slight spinal arthritis in the upper dorsal region. Re-examination two weeks after the original complete neurologic examination revealed a small saddle-shaped area over the lower sacral region with changes which suggested a primary cord tumor. Two other consultants believed that the lesion on the penis was associated with the spinal condition. I held out against this because I did not believe that it was possible for a tumor to escape into the spine or cord without involving the regional lymph nodes.

Dr. Oldberg explored the spine and found bony involvement. Dr. Jaffe, after examination of both specimens, stated that the bone lesion was undoubtedly a metastasis from the small tumor of the foreskin.

DR. J. DELLINGER BARNEY (Boston, Mass.): I haven't any figures immediately at hand, but nearly thirty years ago I looked up a large series of cases of cancer of the penis and reported on them at great length. I found that there were a certain number of cases (I can't remember the figures) in which the glands had been dissected and found to be perfectly negative as regards metastatic cancer, and the patients had died subsequently of metastatic diseases of the liver. Some of those autopsies, I believe, were detailed at length by other writers, and one or two we had at our hospital, but I think they serve to answer Dr. O'Conor's question, and show that one can get metastases through the deep lymphatics of the penis under the pubic arch without involvement of the inguinal glands.

I may say a word in regard to Dr. Graves' suggestion that the penis, when amputated close to the symphysis, creates inconvenience and unhygienic conditions. That is true to a certain extent, but those conditions can be alleviated by furnishing the patient with some kind of a hollow tube, like a section of bamboo or, as in some

instances, an empty bicycle handle which is simply applied to the dimple and used during the functioning of the bladder.

DR. CHARLES M. MCKENNA (Chicago, Ill.): In 1930 before this society we presented a series of cases of carcinoma of the penis. Our conclusions were about the same as those of Dr. Graves. We believe that partial amputation is the better of the two. I think it is most important that one pay considerable attention to the lymph nodes. By that I mean it is not necessary to remove the lymph nodes surgically, but to treat them with the intelligent use of x-ray. In our series of cases the patients who had a partial amputation done always recuperated faster and lived longer, and x-ray treatment was given immediately following operation. Here I would like to emphasize just one point, that if too much x-ray therapy is employed it is just as harmful as where a total or radical operation is made, because it breaks down all resistance and metastasis occurs earlier. I think Dr. Graves presented a concise and very interesting paper.

DR. ROGER C. GRAVES (Boston, Mass.): I have nothing to say except to thank the discussors and to agree with Dr. McKenna that the partial amputation is to be preferred where it can be performed Of course, one is influenced by the extent of the growth.

PRESIDENT'S REMARKS

PRESIDENT CAULK: Gentlemen, the sweetest year of my medical life is coming to a close. I want to let you fine fellows know how deeply I appreciate your wonderful consideration of my many inefficiencies. While my gray matter doesn't function sometimes, my heart is always in the right place, I'll assure you of that.

Now I wish to express my appreciation to all the committees which have functioned so diligently during the year for the great work they have done, and for their coöperation; also to our Secretary. I do appreciate what he has done for me during the year, and I am very happy to see him with us again.

Now comes the great feature of the occasion, the installation of our new President. I want his golf opponents, Dr. Hinman and Dr. Bugbee, the only opponents he ever will have during his administration, to escort him to the chair to allow me to greet him properly.

Dr. Hinman and Dr. Bugbee escorted Dr. Bryan to the platform. (Applause.)

PRESIDENT CAULK: Gentlemen, I introduce to you our dear friend, Dr. Bryan. I know of no man in the world that I would rather have succeed me than this grand fellow. I know that this Association will pass through an era of great security in his tender hands. (Applause.)

Dr. Bryan, the newly elected President, took the chair. (Applause.)

PRESIDENT BRYAN: Gentlemen, I had a speech written of thirty-five minutes' duration, and with your permission, I will be very glad to read it to you. Well, I won't read it, then.

I do want to thank you. I think each and all of you know how one appreciates this chair. I can hardly tell you how I do feel about it, but I feel it is tempered with a very decided degree of inefficiency and unworthiness on my part. I am quite sure, as Dr. Caulk just said, with the guidance and help of our Secretary, that

the Society will go on enjoying its years of success and recognition which it has established in the past.

Again I thank you very much. (Applause.)

Is there anything further? If not, gentlemen, I hope, having had such a successful meeting this year and such a large attendance, we will have the same next year.

The meeting is adjourned.

The meeting adjourned at one-twenty o'clock.